Differentiating between networks associated with linguistic processing: A magnetoencephalographic investigation

Thesis

Differentiating between networks associated with linguistic processing: A magnetoencephalographic investigation.

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Abstract

Many models of reading differentiate between linguistic processing pathways. The studies reported within this thesis demonstrate how magnetoencephalography (MEG), together with the analysis technique Synthetic Aperture Magnetometry (SAM) can be used to investigate spectral power changes associated with different processing routes, with millisecond resolution.

To isolate different linguistic processes, two approaches have been taken. In the first study task manipulations were used to focus attention on either the semantic or phonological nature of a stimulus. Results suggest a task-specific dissociation between the spatial-temporal dynamics of frontal (inferior frontal and BA10) and temporal (BA20) / parietal (BA39/40) effects, which has implications for theories regarding the interaction between frontal "executive" systems and semantic / phonological "stores".

This approach was extended by investigating task-specific effects associated with the priming of the two tasks, prior to stimulus processing demands. Similiarities were observed between these effects and those observed during stimulus processing in terms of location, latency and frequency band, suggesting that task priming may allow investigation into the neural correlates of semantic and phonological processes in the absence of confounds associated with task demands and the choice of stimuli.

The second approach involved the use of stimulus manipulations, within the context of a lexical decision task. Different types of word and nonword vary in terms of their semantic and phonological nature, and therefore in the extent to which they engage semantic and phonological processes. Differential effects were observed between the stimulus conditions, and interpreted in terms of differing degrees of semantic and phonological processing. As each of these approaches have methodological advantages and disadvantages, the results of the stimulus manipulation study are compared to those of the task manipulation study.

Therefore, using three different approaches (task manipulations, stimulus manipulations, and task priming), MEG has been used to differentiate between networks associated with linguistic processing, within the domains of space, time and frequency.

Acknowledgements

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Chapter 1
Introduction

Language has been described as "one of the most important cognitive functions because it is central to our social, intellectual and emotional functioning" (Stowe, 1999, page 1). However, it has been argued that much of the research into the structure and functioning of the language system has "ignored the fact that language is seated in the brain" (Brown & Hagoort 1999, page 3). Similarly, with the development of advanced and sensitive brain-imaging technology, the importance of combining a cognitive neuroscience approach to language with that of linguistic and psycholinguistic research has been stressed (Brown & Hagoort 1999).

This is the approach that has been adopted within this thesis. The studies reported here employ the use of magnetoencephalography (MEG) and Synthetic Aperture Magnetometry (both of which are described in Chapter 2). Using these techniques it is possible to determine task specific spectral power changes (Event Related Synchronisation, ERS and Event Related Desynchronisation, ERD) that are either evoked (phase-locked to stimulus onset) or induced (not phase-locked to stimulus onset). This is believed to be particularly advantageous for the investigation of higher level cognitive processes, such as language processes, as for these tasks timing has been found to be inherently variable, and therefore poorly phase-locked to the stimulus across trials (Michalewski, Prasher & Starr 1986). Within the studies reported within this thesis, MEG was used to differentiate between networks associated with linguistic processing, and specifically those associated with semantic and phonological processes (as discussed in Chapter 3).

Using MEG, together with the analysis technique Synthetic Aperture Magnetometry (SAM), it was possible to characterise these effects in the domains of space, time and frequency. This extends the approach taken within haemodynamic imaging studies such as fMRI and PET (as discussed within Chapter 3), which enables identification of discrete areas of activation associated with specific cognitive processes as it additionally enabled investigation into the time course of these processes, with millisecond temporal resolution, together with the identification of frequency-specific changes in oscillatory power. Frequency effects have been linked to network complexity and synaptic parameters (Brunel & Wang, 2003), and research has investigated the functional significance of brain rhythms (Neuper & Pfurtscheller, 2001; Başar, Başar-Eroglu, Karakaş & Schürmann, 2001), for example in perceptual binding (as reviewed in

Hari & Salmelin, 1997) and attention (Pulvermüller, Birbaumer, Lutzenberger & Mohr, 1997). Within the studies reported within this thesis, frequency-specific oscillatory power changes were observed, however interpretation will concentrate on the anatomy and temporal sequencing of these effects.

In order to isolate semantic and phonological processes, two approaches have been adopted. Task manipulations have been used in order to focus attention on either the semantic or phonological nature of a stimulus (this literature is reviewed in Chapter 4), and stimulus manipulations have been used as different types of word and nonword vary in terms of their semantic and phonological nature, and presumably in the extent to which they engage semantic and phonological processes (this literature is reviewed in Chapter 8).

Chapter 5 reports a study in which the task manipulation approach was adopted. There were two task conditions, a semantic task which involved making a living/nonliving decision, and a phonological task which involved counting the number of syllables contained within a word.

This task manipulation approach was extended within a study which investigated task-specific effects associated with the priming of either a semantic or phonological task using task cues presented prior to presentation of the target stimulus (as reported in Chapter 7). Effects were observed within the epoch associated with the presentation of the task prime and compared to those observed within the epoch associated with the presentation of the target stimulus. This extends the work on the priming of semantic and phonological tasks. It also extends the findings relating to task dependent differential effects observed in response to a task cue, as it considers these effects alongside those associated with task-specific stimulus processing, and identifies a number of parallels between the two.

A study in which the stimulus manipulation approach was adopted, within the context of a lexical decision task, is described in Chapter 9. Participants were required to perform a lexical decision task using six different stimulus types, three were word categories and three were nonword types (pronounceable pseudowords, nonpronouncable consonant strings, and strings of symbols). Attempts are made to interpret the MEG data within the context of reaction time data, the results of previous task manipulation studies, and the results of the task manipulation studies reported in Chapters 5 and 7 (as discussed in Chapter 10), in order to evaluate the consistency between the two approaches.

Chapter 2

Magnetoencephalography.

The outmost layers of the brain, the cerebral cortex, contain a complex network of at least 10^{10} neurons, with 10^{14} interconnections or synapses (Hämäläinen, Hari, Ilmoniemi, Knuutila & Lounasmaa, 1993). Information processing within the brain is associated with the movement of electrical currents within this network. In 1924 Hans Berger discovered that potential differences generated by these currents can be measured on the scalp (Berger, 1929). This forms the basis of the recording technique electroencephalography (EEG). More recently, it was discovered that the magnetic fields generated by these currents can also be detected outside the head, using superconducting quantum interference devices (SQUIDs) (Cohen, 1968). Magnetoencephalography (MEG) is a noninvasive brain imaging technique that involves the measurement of these weak magnetic fields (~fT) using multichannel SQUID systems. On the basis of these magnetic field measurements it is possible to draw conclusions regarding the functional organisation of the human brain, and the functional properties of the active brain areas (Okado, 1982).

This chapter begins with a discussion about the neural basis of these magnetic fields, followed by a description of the signal detection process, and the ways in which the signal-to-noise ratio can be optimised. MEG is then compared to other recording techniques, and different approaches to data analysis are discussed, together with their associated assumptions. The chapter ends with a consideration of the analysis techniques used within this thesis.

2.1, The neural basis

In the neuron's resting state, there is a –70mV potential difference across the cell membrane (the inside of the neuron being negatively charged). An "action potential" is a propagating excitation that occurs within an "active" neuron. During the "depolarisation" phase the cell membrane selectively admits Na^+ ions, increasing the inside potential to +30mV. The membrane permeability then changes allowing an outward flow of K^+ ions ("repolarisation"), which restores the original potential. The movement of these ions gives rise to three types of current. As the positively charged ions enter the cell, intracellular (primary) currents (figure 2.1) are brought about by the repulsion of positive ions already within the cell. These currents are directed away from the region of the synapse. This advancing accumulation of positive charge gives rise to transmembrane displacement

currents. These transmembrane currents make a negligible contribution to the field relatively far from the neuron, due to their radial symmetry (Okada, 1982). The transmembrane currents in turn repel positive ions in the extracellular space, which produces extracellular (volume) currents (figure 2.1). Volume currents are established to close the current loop, in line with the conservation of electric charges. The duration of an action potential is of the order of milliseconds.

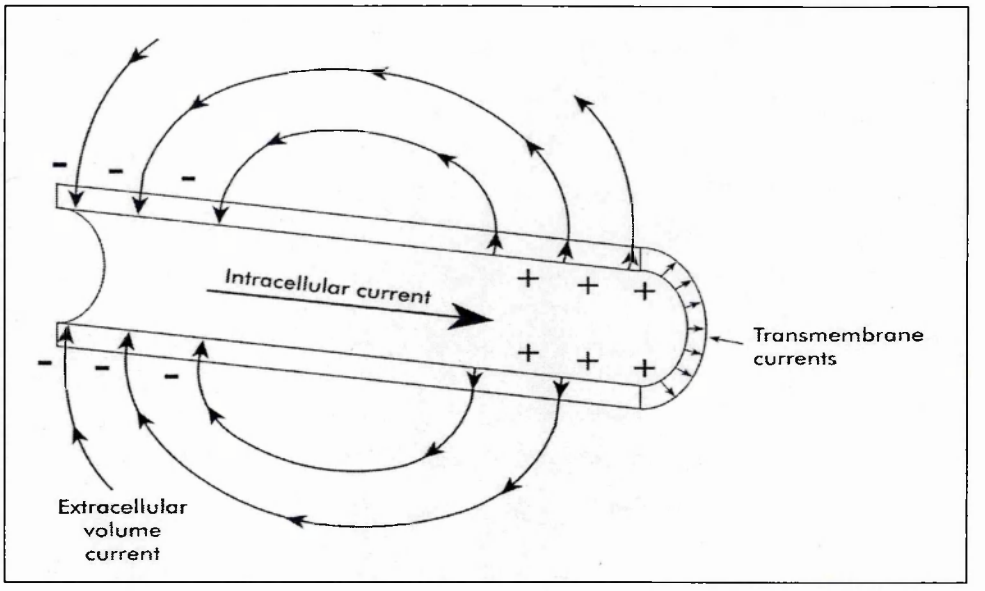


Figure 2.1, The intracellular, transmembrane and extracellular currents associated with an action potential (from Lewine & Orrison, 1995).

When an action potential reaches a synapse, there is an accumulation of positive charge at the presynaptic membrane due to the intracellular current. This triggers the release of neurotransmitters, some of which diffuse across the synaptic cleft towards the postsynaptic membrane (figure 2.2). The ionic flow across the synapse, the postsynaptic potential, gives rise to a current distribution that has a typical duration of 10 -100ms.

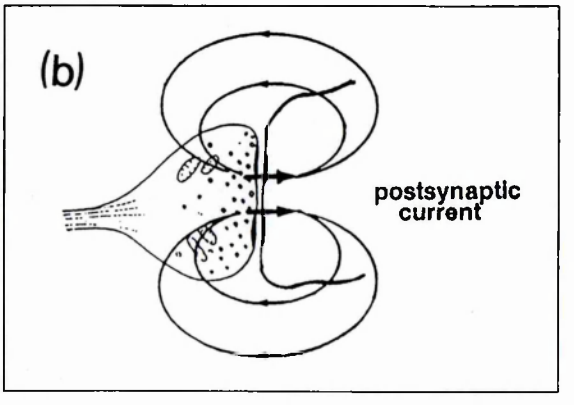


Figure 2.2, Currents associated with postsynaptic activity (from Pizzella & Romani, 1990).

Whereas the postsynaptic potential can be described as a current dipole, the action potential can be represented by a quadrupole. Magnetic field strength decreases more rapidly with distance for quadrupoles than for dipoles. This suggests that postsynaptic potentials are the main source of magnetic fields detected outside the head. Similarly, the

longer time scale of postsynaptic potentials would also suggest that temporal summation would be more effective for postsynaptic potentials than for action potentials.

It is believed that approximately 10^4 to 10^5 adjacent neurons must be active at the same time in order for there to be measurable changes in the magnetic field outside the head (Vrba & Robinson, 2001). The main contributors of detectable magnetic fields are thought to be pyramidal cells, which are arranged in palisades in the cortex so that their postsynaptic electrical fields sum across an active area.

2.2. Signal detection

SQUIDS are sensitive detectors of magnetic flux, based upon the Josephson effect whereby electrons can tunnel through a resistive barrier between two superconducting regions. The dc SQUID takes the form of a loop of superconducting wire containing two weak links. These SQUIDs are positioned in a dewar containing liquid helium. At a temperature of 4K the SQUIDs are superconductive. The magnetic flux from the head is inductively coupled into the SQUID via a pickup coil (figure 2.3). The voltage across the SQUID changes with change in flux such that output voltage is a periodic function of the applied flux. This voltage is used to generate a feedback current which is coupled back into the SQUID loop to null the applied signal flux. The feedback current is a direct measure of the change in the magnetic flux applied to the SQUID (see Hämäläinen et. al. 1993 for details).

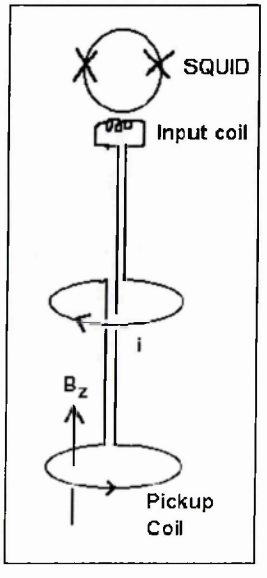


Figure 2.3. The radial component of the magnetic flux from the head (Bz) induces a current (i) within the pickup coil of the gradiometer. The magnetic flux is inductively coupled into the SQUID (from http://www.nottingham.ac.uk/physics/ugrad/courses/mod_home/f31ab1/notes/MEGFMRI.doc).

2.3. Noise reduction

The magnetic fields detectable outside the head are typically 100 million times smaller than the earth's magnetic field and one million times smaller than the magnetic fields produced in an urban environment (figure 2.4). Therefore the signal to noise ratio needs to be optimised.

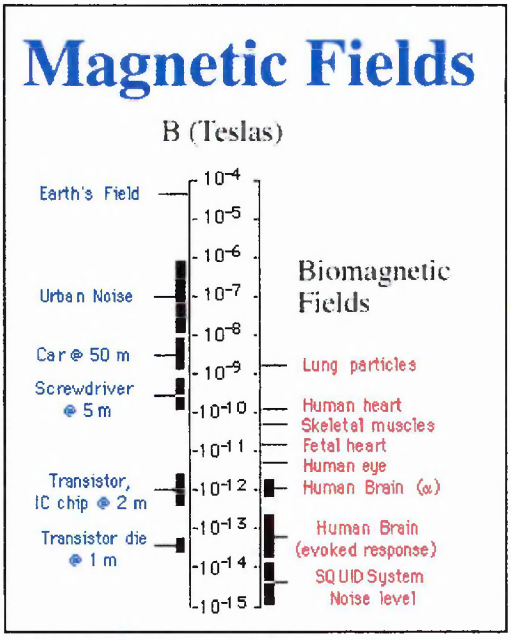


Figure 2.4. The strength of magnetic fields produced by the brain with respect to magnetic fields produced by various biological and environmental sources, showing that the magnetic fields that are measured in MEG are 100 million times smaller than the earth's magnetic field and 1 million times smaller than the magnetic fields produced in an urban environment (from http://www.nottingham.ac.uk/physics/ugrad/courses/mod_home/f31ab1/notes/MEGFMRI.doc).

The field of a magnetic dipole is inversely proportional to the square of the distance between the dipole and the sensor. Therefore the field from a distant source is relatively uniform in direction and magnitude at the pickup coil. First order gradiometers consist of two identical loops that are connected in series, and wound in opposite directions (figure 2.3). Distant sources will couple equally to both coils and therefore the coils will produce a signal of equal strength, but opposite sign, resulting in there being no net signal. A magnetic dipole that is much closer to one coil than the other will couple better to the closer coil. In this way the signal to noise ratio can be improved.

To further reduce the effects of external fields, MEG systems are typically placed within a magnetically shielded room. These consist of layers of mu-metal (for low frequency shielding) and aluminium (for high frequency shielding), which act as passive shielding. Active shielding involves the generation of currents to produce fields that oppose those detected outside the shielded room (Holmlund, Keipi, Meinander, Penttinen & Seppä, 2000).

Averaging techniques also serve to improve the signal to noise ratio. These will be discussed later within this chapter.

2.4, MEG compared to other techniques

Neuronal activity induces localised changes in blood flow and oxygenation levels. These can be investigated using imaging techniques such as functional Magnetic Resonance Imaging (fMRI) (Ogawa, Tank, Menon, Ellermann, Kim, Merkle & Ugurbil, 1992), which measures the indirect effects of neural activity on local blood volume, flow and oxygen saturation, and Positron Emission Tomography (PET) which measures tissue metabolic rate. Although these techniques can produce images that have a spatial resolution in the order of millimetres, the temporal resolution for fMRI is approximately one second, and for PET is in the order of minutes. These techniques involve exposing the individual to time-varying strong static magnetic fields in the case of fMRI, and radioactive tracers in the case of PET. It has also been argued that the blood oxygenation level dependent (BOLD) changes detected by fMRI do not necessarily directly correspond with regions of electrical neuronal activity, because of the complex relationship between BOLD changes and the underlying neural activity (Baillet, Mosher & Leahy, 2001).

Both EEG and MEG are noninvasive techniques that can be used to record physiological signals in the millisecond range. Passive compensatory currents (volume currents) associated with postsynaptic activity produce potential differences across the scalp that can be measured using EEG. The amplitudes of these currents are attenuated by the poorly conducting skull. Also, due to the inhomogeneous conductivity of the skull, the surface current distribution is distorted; this gives rise to a smearing effect.

If the axis of a gradiometer is oriented perpendicular to the head (and the head is modelled as a spherically symmetric volume conductor) so that it measures the radial component of the magnetic field, then the measured magnetic field will be associated primarily with the intracellular currents. The extracellular current is believed to contribute negligibly to the magnetic field measured on the scalp (Okada, 1982). In a spherically symmetric volume conductor, the radial component of the magnetic flux density is independent of the conductivity and the number of layers of the volume conductor, so that source localization should be more accurate for MEG than EEG.

It has been argued that whereas EEG may be more sensitive to radially oriented dipoles, MEG is primarily sensitive to tangentially oriented dipoles (or the tangential component of any dipole) (Rose & Ducla-Soares, 1990) because a radially oriented dipole in a conducting sphere does not produce a magnetic field outside of the sphere. This has lead to the assumption that MEG is insensitive to gyral sources. However, by analytically computing the probability of detecting a source at different regions and orientations, it has been reported that source depth rather than orientation is the main factor that compromises MEG sensitivity (Hillebrand & Barnes, 2002). Although thin (approximately 2mm wide) strips of poor resolvability were found at the crest of gyri, these strips were surrounded by regions of high resolvability, and it is argued that such strips could only account for a relatively small proportion of an active area.

2.5, The forward problem

Given certain assumptions, source positions and strength parameters, the magnetic field in the MEG sensors can be computed (the forward problem). A solution for the forward problem can be derived from Maxwell's equations. Sarvas (1987) shows that if a homogeneous spherical head model is used, the forward model reduces to Equation 1, where B represents magnetic flux density (T) due to a current dipole source with moment Q. r represents the point of measurement, and r_0 the location of the current dipole source, relative to the origin of the co-ordinate system. μ_0 is the permeability of free space. This shows magnetic flux to decrease as a function of the squared distance from the source.

$$\boldsymbol{B}(\boldsymbol{r}) = \frac{\mu_0}{4\pi F^2}\left(F\boldsymbol{Q}\times\boldsymbol{r}_0 - \boldsymbol{Q}\times\boldsymbol{r}_0\cdot\boldsymbol{r}\nabla F\right) \qquad \textbf{Equation 1.}$$

where $F = a(ra + r^2 - \boldsymbol{r}_0\cdot\boldsymbol{r})$, $\nabla F = (r^{-1}a^2 + a^{-1}\boldsymbol{a}\cdot\boldsymbol{r} + 2a + 2r)\boldsymbol{r} - (a + 2r + a^{-1}\boldsymbol{a}\cdot\boldsymbol{r})\boldsymbol{r}_0$.
$\mathbf{a} = (\mathbf{r} - \mathbf{r}_q)$, $a = |\mathbf{a}|$, and $r = |\mathbf{r}|$.

It is argued that such spherical head models work well for MEG measurements, as primary currents are less affected by deviations from the idealized head model than volume currents (Baillet, Mosher & Leahy, 2001). Alternatively more realistic head models can be obtained by extracting the surface boundaries for the brain, skull and scalp from anatomical images produced using magnetic resonance imaging (MRI), or X-ray computed tomography (CT) imaging. This information can then be used in a boundary element method (BEM) (for example, Crouzeix, Yvert, Bertrand & Pernier, 1999), a finite element method (FEM) (for example, Broek, Reinders, Donderwinkel and Peters, 1998) or using a multisphere model, in order to provide a solution for the forward model.

2.6, The inverse problem

The inverse problem refers to the estimation of primary currents from magnetic field measurements outside the head. Algorithms that address this tend to try to minimize the difference between the measured data and that predicted by forward solutions. However, in this context the inverse problem is "ill-posed" as there is no unique solution. Many different source configurations could produce exactly the same measured magnetic field. Therefore assumptions need to be made, for example, these can take the form of spatial constraints based upon a reconstruction of the cortical surface from the Magnetic Resonance Image (MRI) (Hillebrand & Barnes, 2003). There are three main approaches; dipole fitting, distributed source techniques, and beamforming. These approaches are discussed below, focusing on the assumptions that are made, and their strengths and weaknesses.

2.7, Source localisation

2.7.1, Current dipoles

The equivalent current dipole model has been described as "the oldest and most frequently used model for brain source activity" (Vrba, 2002). This model makes the assumption that neural activity can be represented by a point source, or a set of sources, that represent the primary current associated with the combined activation of a larger number of neurons. A current dipole is described in terms of position, orientation and strength. Figure 2.5 shows a current dipole, the magnetic field associated with it, and a topographic map.

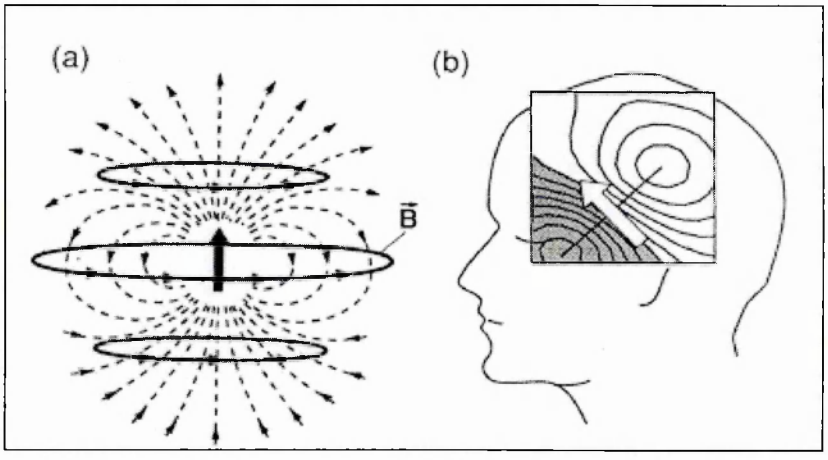


Figure 2.5. An equivalent current dipole. a) The primary electrical current (represented by the large arrow), volume current (dashed lines), and the magnetic field associated with it (solid lines). b) An example of a topographic field map calculated from measured MEG signals. From this field map the equivalent current dipole is localised to midway between the two extrema. (Figures taken from Hämäläinen, Hari, Ilmoniemi, Knuutila & Lounasmaa, 1993).

Multiple dipole analysis involves guessing the number of dipoles and their initial positions and conducting a search that minimizes differences between the field computed from the dipoles and the measured field (for example, a least-square fit). The model can be applied to a single time point, or over a time window. A "moving dipole model" involves optimisation over a set of times slices individually so that the location and orientation is not constrained. "Fixed dipole models" involve optimisation over a time window so that dipole locations and orientations are fixed for the whole time interval, but the magnitude varies. "Rotating dipole models" involve a fixed dipole location, but the orientation varies (Mosher, Lewis & Leahy, 1992). Although it has been argued that it is "still an open question as to which model describes brain sources best" (Huang, Aine, Supek, Best, Ranken & Flynn, 1998), most of the dendrites of pyramidal cells are oriented perpendicular to the cortical surface, so it seems physiologically valid to restrict the dipole orientation so that it is perpendicular to the cortical surface.

There are problems associated with the manual selection of starting parameters such as the first guess dipole locations and orientations. If the first guess lies within a local minimum, the global minimum may not be found. In order to improve the accuracy of this procedure automated processes have been developed such as the "multi-start downhill simplex method" which runs hundreds to thousands of searches using randomly selected initial starting parameters (Huang et. al. 1998). It has been reported that such multistart

MEG analysis procedures have been found to localise multiple regions of activity and characterise their time course reliably (Aine, Huang, Stephen & Christner, 2000), despite being computationally intensive.

One of the main problems associated with dipole fitting is that the number of sources to be used has to be decided upon a priori. Various strategies have been employed in order to determine an adequate number of dipoles, such as the singular value decomposition technique described by Huang et. al. (1998). It is also argued that in practice analysis is often done using several dipole models and the most physiologically plausible results selected (Baillet, Mosher & Leahy, 2001). An alternative approach is to use a distributed source model, which does not require the number of sources to be determined a priori.

2.7.2, Distributed source models

Within the distributed source framework a source is considered to be an array of current elements. One example is the minimum norm estimation (MNE) (Hämäläinen & Ilmoniemi, (1994). This approach involves placing dipolar sources at each node on a grid, for example, on the cortical surface, and determining the source strength for each of these sites. The solution of least power that accounts for the data is reconstructed. It has been argued that as misleading results can be obtained if the current dipole assumptions are invalid, MNE is the best estimation of the current when minimal a priori information about the source is available (Hämäläinen & Ilmoniemi, 1994).

Small currents that are close to the detectors can produce fields of similar strength to those produced by larger currents at greater depths. Finding the solution of least power, tends to lead to superficial source distributions. In an attempt to compensate for this, weighted minimum norm estimates (wMNE) are sometimes used (depth normalization). Figure 2.6 shows an example of MNEs for a visual experiment (Ahlfors, Ilmoniemi & Hämäläinen, 1992). The MNEs were calculated using the assumption that the primary current lies on a spherical surface placed 10mm below the scalp.

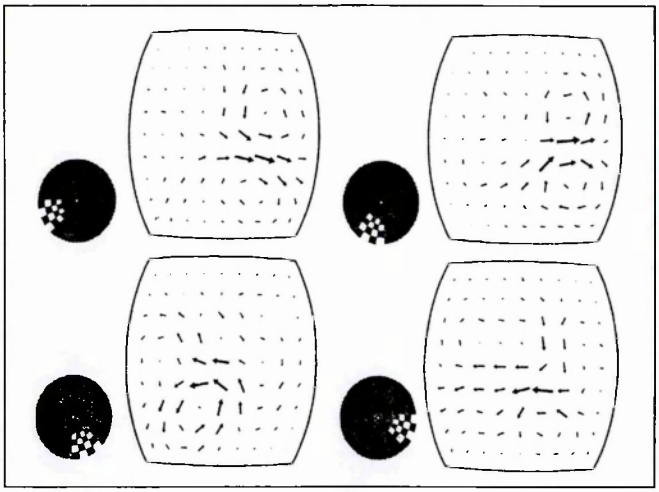


Figure 2.6. An example of MNEs for a visual experiment involving the presentation of a parafoveal pattern in different octants (Ahlfors, Ilmoniemi & Hämäläinen 1992). The stimuli are shown to the left of each current estimate. The results show that for left visual field stimuli the primary current is on the right, and that for right visual field stimuli the primary current is on the left (from Hämäläinen & Ilmoniemi, 1994).

This approach has also been criticised on the grounds that it is highly underdetermined (there are more unknown parameters than MEG measurements), the results often appear smeared, and the constraints are mathematical rather than physiologically justified (Aine et. al. 2000).

However, it has been argued that the assumptions made within low resolution brain electromagnetic tomography (LORETA), an example of a distributed source technique, are physiologically justified (Pascual-Marqui, Esslen, Kochi & Lehmann, 2002). With this technique a collection of voxels can be used to model, for example, the cortex, and the solution is determined by imposing the constraint that neuronal activity at each voxel has maximum similarity (in terms of orientation and strength) with that of adjacent voxels. It is argued that this constraint is consistent with physiology as a high degree of synchronization of neighbouring neurons is necessary for spatial summation to produce extracranially measurable fields (Pascual-Marqui et. al. 2002).

The focal underdetermined system solution (FOCUSS) is an example of an iterative re-weighting distributed source technique which begins by producing an initial distributed estimate, and recursively enhances the values of some of the initial solution elements, while decreasing the rest until they become zero. It has been reported that such a technique produces high resolution solutions appropriate for highly localised sources (Gorodnitsky, George & Rao, 1995), although it has also been argued that the final solution tends to be highly dependent upon the initial estimate (Hillebrand, 2000).

2.7.3, Beamforming techniques

Beamforming techniques involve spatially filtering the data from a sensor array to discriminate between signals originating from an area of interest and those from other areas. A beamformer effectively monitors a particular region, and blocks the contribution from other brain regions. This has an advantage over least-squares methods in that it enables sources to be found by sequentially scanning through the possible set of locations and orientations, rather than searching simultaneously for a predetermined number of sources.

Beamformer techniques differ from dipole fitting techniques in a number of ways. For example, the risk of being trapped in a local minima is avoided by scanning a region for all possible sources. An a priori estimate of the number of sources is not required, and instead of minimizing the difference between measured and modelled data, a minimum power constraint is imposed.

Beamformer techniques rely upon the assumption that each possible source has a unique time course. Sources that are perfectly synchronous cannot be detected. The beamformer weights are selected so that the overall output of the beamformer is a minimum. This is achieved by minimising the contribution that noise, or other brain sources, makes to the beamformer output. If another brain (noise) source is correlated to the source at the target location, then removing/minimising the signal from the noise source would also remove the signal from the target source (since their signals are correlated). However, for sources to be invisible to the beamformer, they would have to maintain perfect synchrony throughout the entire time course of the experiment (Singh, Barnes, Hillebrand, Forde & Williams, 2002), and it has been reported that two sources can be resolved at relatively large temporal correlation levels (Van Veen, van Drongelen, Yuchtman & Suzuki, 1997). These techniques have also proved to be successful within many experimental paradigms, such as those involving sensory, motor, and cognitive tasks (Cheyne, Barnes, Holliday & Furlong, 2000; Taniguchi, Kato, Fujita, Hirata, Tanaka, Kihara, Ninomiya, Hirabuki, Nakamura, Robinson, Cheyne & Yoshimine, 2000; Singh et. al. 2002), suggesting that the assumptions are reasonable.

Despite the assumption of uncorrelated sources, beamformer techniques have a number of advantages over other imaging methods. They do not rely on a priori estimates

of the number of sources, as in dipole fitting, and there is no tendency for sources to float to the surface as in minimum norm solutions.

One example of a beamforming technique is the multiple signal classification (MUSIC) algorithm. Within this approach a probe dipole is placed at every node of a pre-determined grid positioned over the brain. At each grid point the contribution of each dipole to the measurements is evaluated. This results in a series of MUSIC values from which peaks can be identified. One of the problems associated with this technique is that errors in initial source localisation will affect the ability to subsequently localise other sources. Recursively Applied and Projected (RAP) MUSIC (Mosher & Leahy, 1999) involves the recursive estimation of multiple sources, and can be used to overcome this problem.

The beamforming analysis technique Synthetic Aperture Magnetometry (SAM) (Robinson & Vrba, 1999; Van Veen et. al. 1997) was used to analyse the data presented within this thesis. A recent MEG study used data produced from a dipole phantom in order to compare the results obtained using dipole fitting, MUSIC and SAM (Robinson & Vrba, 2000). It was reported that while both MUSIC and SAM were found to localise the phantom dipole more accurately than the simple dipole fit, unlike SAM, MUSIC occasionally identified spurious peaks, and for one of the sources produced fluctuating results. SAM localised the source with a smaller localisation uncertainty.

In the next section SAM will be discussed, and the advantages of using this technique will be considered. Finally the methods used within this thesis will be outlined, in particular the averaging of SAM images, the use of permutation testing to assess the statistical significance of SAM results, and the use of time-frequency analysis.

2.8, Synthetic Aperture Magnetometry (SAM)

Synthetic Aperture Magnetometry (SAM) is a beamforming technique for MEG data analysis, based upon the same principle of fixed array weighted channels as found in modern radar systems (Van Veen & Buckley, 1988). The method works as follows: An individual's MRI is divided into voxels of predetermined size (typically 0.5 cm^3). The amplitude of the electrical current within each voxel is estimated from a weighted sum of the MEG sensors (Figure 2.7). The time resolution is in the order of milliseconds. The output of the spatial filter can therefore be thought of as a virtual electrode placed at the neuronal source location (Barnes & Hillebrand, 2003).

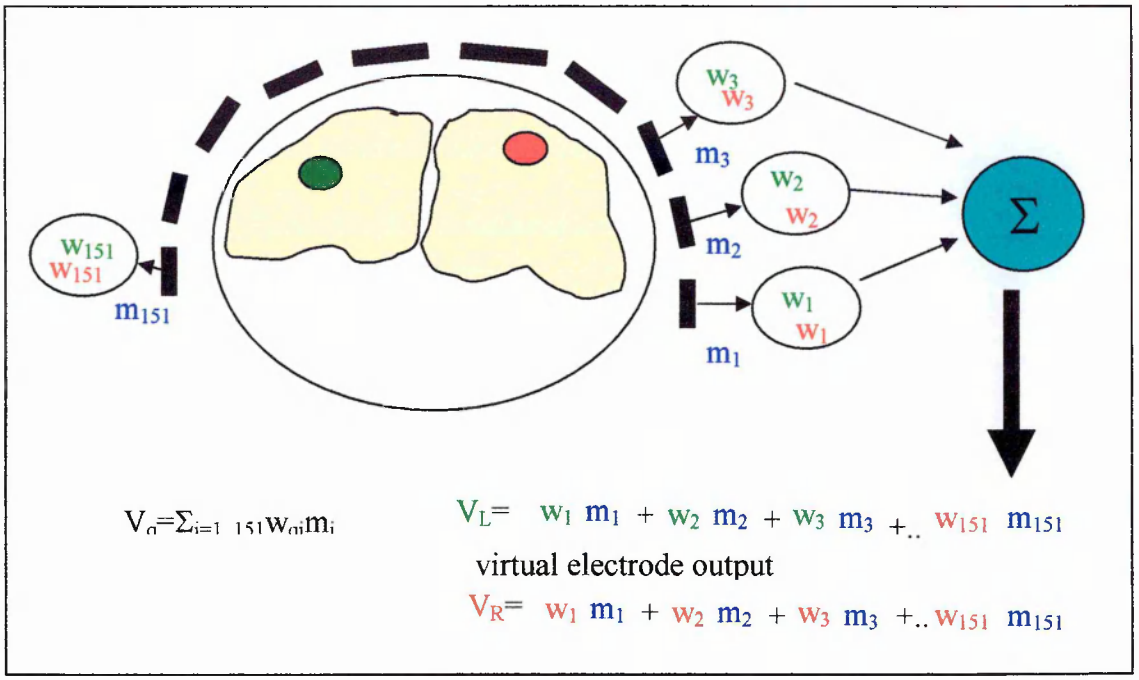


Figure 2.7. The figure shows how the beamformer approach can be used to estimate the amplitude of electrical current at different locations within the brain. Two sources are shown, one in the left hemisphere (shown in green) and one in the right hemisphere (shown in red). For each of these source locations an optimal set of weights can be calculated (w_1, w_2, w_3 etc.). The weights are designed to increase the sensitivity to signals from the location of interest while reducing the contribution from sources at other locations (which are treated as noise). The beamformer output can be computed by multiplying the output of each sensor (m) by the corresponding weighting coefficient (w) and summing these values in order to estimate the electrical current at the source location (V_L for the left hemisphere source and V_R for the right hemisphere source) with millisecond resolution. The output can therefore be thought of as that of a virtual electrode (V) placed at a neuronal source location (from personal communication Barnes, 2001).

Fourier analysis can be used to calculate the total amount of power in each frequency band for a certain time window. For each voxel, the spectral power change between pre-defined active and passive time windows can be assessed, and a statistical estimate (pseudo-t-test) determined (Robinson & Vrba, 1999). By conducting this analysis for all possible voxels, the brain can be systematically scanned in order to produce a three dimensional statistical parametric map for the whole brain. In this way, for specific time and frequency windows, oscillatory power increases and decreases can be observed relative to a control state.

The most common experimental paradigm for MEG is the evoked-response, whereby the response to many stimulus presentations is averaged. This increases the signal

to noise ratio, and means that only cortical activity that is tightly phase-locked to the initial stimulus presentation can be investigated. SAM enables observations to be made in terms of the ongoing activity between two states.

The observed effects relate to frequency specific changes in cortical oscillatory power. Power increases are referred to as "event-related synchronisation" (ERS), and power decreases termed "event-related desynchronisation" (ERD) (Pfurtscheller & Lopes da Silva, 1999). ERS and ERD effects can either be evoked (phase-locked to the stimulus), or induced by the presence of the stimulus (without phase-locking). This is believed to be particularly advantageous for the investigation of higher level cognitive processes, such as language processes, as for these tasks timing has been found to be inherently variable, and therefore poorly phase-locked to the stimulus across trials (Michalewski, Prasher & Starr, 1986).

2.8.1. Event Related Synchronisation (ERS) / Event Related Desynchronisation (ERD)

ERD has been described as a "correlate of an activated cortical area (Pfurtscheller, 2001, page 1257), and lower alpha ERD has been interpreted as being linked to increased attention and alertness (Pfurtscheller & Lopes da Silva, 1999), and has been found to increase with task complexity (Sterman, Kaiser & Veigel, 1996) and task difficulty (Karrasch, Krause, Laine, Heikki Lang & Lehto, 1998). ERD has been observed within a range of cognitive paradigms (Dujardin, Bourriez & Guieu, 1995; Singh, Barnes, Hillebrand, Forde & Williams, 2002) and found to coincide with regions showing an evoked hemodynamic response using fMRI (Singh et. al. 2002), which supports the notion that ERD represents increased neural activation in a cortical area.

In contrast, ERS has been described as the "correlate of a deactivated cortical area" (Pfurtscheller, 2001, page 1257), and indicative of "cortical areas at rest or in an idling state" (Karrasch et. al. 1998, page 112). These interpretations have arisen based upon the results of studies such as those showing post-movement beta ERS within the motor cortex (Stancák & Pfurtscheller, 1997). Within the context of memory research, Klimesch (1996) describes theta ERS as reflecting either a resting state or "a state of functional inhibition" whereby a memory search can be blocked from irrelevant networks (p 61). Similarly, Neuper & Pfurtscheller (2001) describe ERS as representing an "inhibition of ... cortical areas" (page 41).

However, there are a number of problems associated with interpreting ERD and ERS effects in such phenomenological terms. Although, as the name suggests, ERS has been described as resulting from "the cooperative or synchronised behaviour of a large number of neurons" (Pfurtscheller & Lopes da Silva, 1999, page 1852), and ERD as desynchronised behaviour, it has been argued that such a model represents an oversimplification, and fails to explain a number of macroscopic oscillatory effects (Hadjipapas & Barnes, in preparation). In particular, the "cortical idling" interpretation of ERS is criticised based on findings such as those showing occipital alpha ERS to covary and increase in terms of spectral power with increasing task demands (Krause, Heikki Lang, Laine, Kuusisto & Pörn, 1996; Jensen, Gelfand, Kounious & Lisman, 2002).

Although it seems that the functional significance of ERD/ERS effects can only be fully understood once more is known about the functional organisation and the dynamics of the underlying neuronal networks, further possible explanations for the observed ERD/ERS effects are considered within Chapter 7.

2.8.2. Group SAM

Using Statistical Parametric Mapping (SPM99, Friston, Holmes, Worsley, Poline, Frith & Frackowiak, 1995), individual SAM images (which are coregistered with that participant's anatomical MRI) can be spatially normalised and averaged to produce a group image. This allows the salient regions involved in a task to be identified (Singh et. al. 2002), although there is the possibility that effects may be missed due to individual variability. Such an approach was taken in a recent MEG study reported by Singh et. al. 2002). Within this study Group SAM images revealed a power decrease (ERD), during the active phase of both a language and a biological motion experiment, which was found to be spatially coincident with an increase observed in the fMRI BOLD response for the same tasks. It is argued that these results provide a cross-validation of the Group SAM approach with that of fMRI.

The Group SAM results reported within this thesis were obtained using random-effect analysis (rfx). Unlike fixed-effect analysis, random-effect analysis takes into account both within and between subject variance, and can therefore be used to enable inferences to be extended to the population from which the participants were taken (Friston, Holmes, & Worsley, 1999). Group SAM images can be visualised using mri3dx (Singh, undated) and their statistical significance assessed using statistical nonparametric permutation testing, (SnPM).

2.8.3. Statistical nonparametric mapping (SnPM)

Parametric statistics have been applied to fMRI and PET data, for example using a random effects model (Holmes & Friston, 1998). This involves running t-tests using inter-subject variances established from individual maps. However, it has been argued that due to the high inter-subject variances that are associated with ERD and ERS, and the sensitivity to deviations from normality that is associated with small sample sizes, the assumption of a normal statistical distribution for MEG data may be invalid (Singh, Barnes & Hillebrand, 2003). Nonparametric permutation testing allows the statistical significance of voxel effects to be established without assuming that there is a normal distribution (Nichols & Holmes, 2001).

Permutation testing is a form of resampling technique. As opposed to classical parametric tests, which use theoretical sampling distributions, resampling methods compare an observed statistic to a sampling distribution generated from repeated sampling within the same empirical sample. Although the technique has been criticised on the grounds that the resampling is based on only one empirical sample, it has certain advantages in that it does not require parametric distributional assumptions to be met, and it is entirely empirically based.

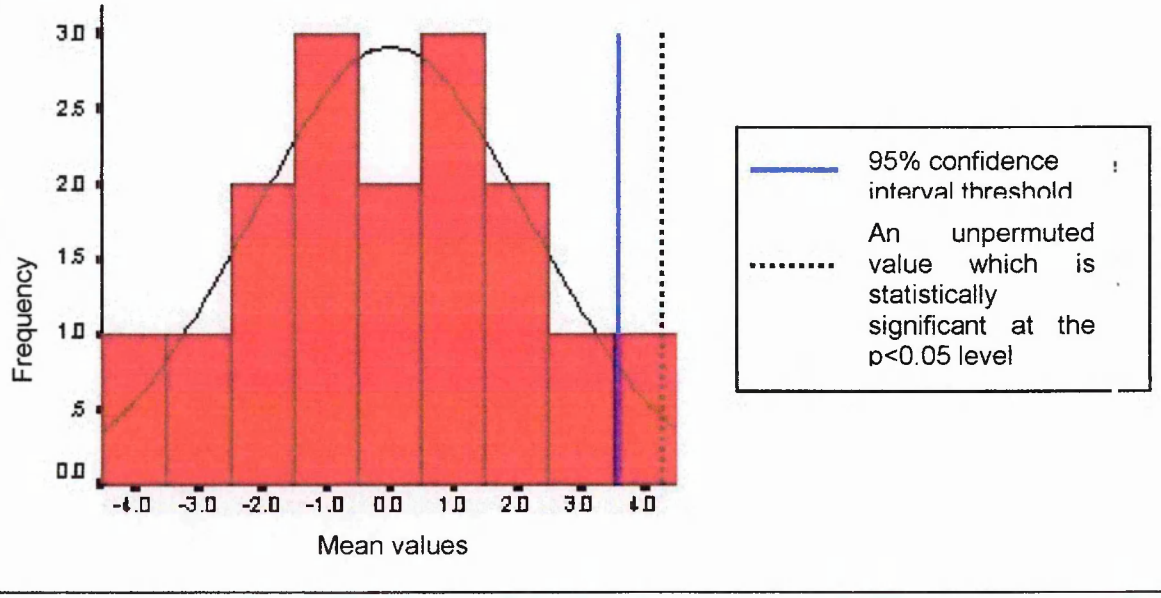
The application of this technique to SAM images has been described by Singh et. al. (2002). An activation map is first produced for each participant, which is then spatially normalised, and a voxel-wise T image is calculated using the inter-subject variances. The statistical significance of the T-score at each voxel is determined by permutation testing. It is assumed that within the activation maps, noise is symmetrically distributed about a mean of zero. If the null hypothesis were true (and there is no significant group activation), then multiplying any of the participants activation values for a particular voxel by –1 will have no effect, the null hypothesis will still be true for that voxel. For each voxel there are 2^N possible combinations of values that can be multiplied by –1 (permutations). Therefore with ten participants, 1024 permutations are possible. Within the studies performed within this thesis 1000 permutations were performed in order to obtain a distribution.

Once the permutations have been performed they are used to form a sampling distribution. The statistical significance of an unpermuted value can be tested against this distribution. For example, a threshold value can be calculated whereby 5% of the

permutations lie above this value. If the unpermuted value lies beyond this threshold then it is possible to state that the probability of this value occurring due to chance is less than 5%. An example is shown in figure 2.8.

Figure 2.8. An example of permutation testing for four participants, which allows 16 permutations to be performed. In this example the t values obtained from the four participants were 2, 3, 4 and 5. The different permutations are represented as different columns in the table). The means obtained from these permutations (shown in the bottom row) are used to create a sampling distribution (as shown by the histogram) against which the significance of unpermuted values can be assessed. In this example the 95% confidence threshold is approximately 3.5. As this unpermuted mean value is greater than this 95% confidence threshold, it is said to be statistically significant ($p<0.05$).

	2	-2	2	2	2	-2	-2	-2	2	2	2	-2	-2	-2	2	-2
	3	3	-3	3	3	-3	3	3	-3	-3	3	-3	-3	3	-3	-3
	4	4	4	-4	4	4	-4	4	-4	4	-4	-4	4	-4	-4	-4
	5	5	5	5	-5	5	5	-5	5	-5	-5	5	-5	-5	-5	-5
Means	4	3	2	2	1	1	1	0	0	-1	-1	-1	-2	-2	-3	-4



This technique can be adapted in order to correct for multiple comparisons. For each iteration, instead of using the T value at each voxel, the largest T value can be recorded and used to generate a probability distribution for the largest T value in the volume. A probability threshold of, for example, 5% can be set for this distribution, so that the probability of any T value in the volume being greater than this threshold by chance is less than, 5%. The results of SnPM analysis presented within this thesis have been corrected for multiple comparisons in this way.

There are certain limitations associated with this approach. Although the gross outline of the brain can be matched by the normalisation procedure, individual sulci and gyri can vary in position by several tens of millimetres (Steinmetz, Furst & Freund, 1990), which could limit the accuracy of group imaging studies. Also, it is possible that significant effects observed in group imaging studies may reflect a weak effect that is highly spatially consistent, whereas stronger effects may fail to reach significance due to spatial variability (Singh et. al. 2002). However widespread ERD/ERS effects associated with induced activity (for example within cognitive paradigms) are less susceptible to these problems than focal, stimulus-driven effects, and it is possible to smooth the SAM images (Hall, Hillebrand, McNab & Barnes, submitted) or the noise variance (Nichols & Holmes, 2001) in order to avoid these problems. Despite these potential limitations, the main advantage of this technique is that it uses a probability distribution that is generated from the data rather than assuming a normal distribution.

For the experiments presented within this thesis, these non-parametric permutation methods were applied using a modification of the nonparametric analysis toolbox (SnPM). Using this technique, maps of significant voxel effects can be produced for specific frequency bands and time windows, allowing the localisation of frequency-specific task-related changes within the cortex.

2.8.4, Time-frequency analysis

In SAM analysis all the time points within an Active or Passive block are used in order to estimate spectral power, so that time resolution is sacrificed to increase frequency resolution and the signal-to-noise ratio. However, the output of the spatial filter (which is a linear sum of the MEG channels) can be thought of as a virtual electrode placed at the neuronal source location, so that the time course of the neuronal activation at each of these locations is given with millisecond resolution. The time-frequency information at these voxels can be further analysed using either moving-window Fourier analysis or Wavelet analysis. This enables the temporal sequencing of activity to be observed within pre-defined Regions of Interest voxels. Individual time-frequency representations are produced for each epoch, and are then averaged. An example time-frequency representation is presented in Figure 2.9.

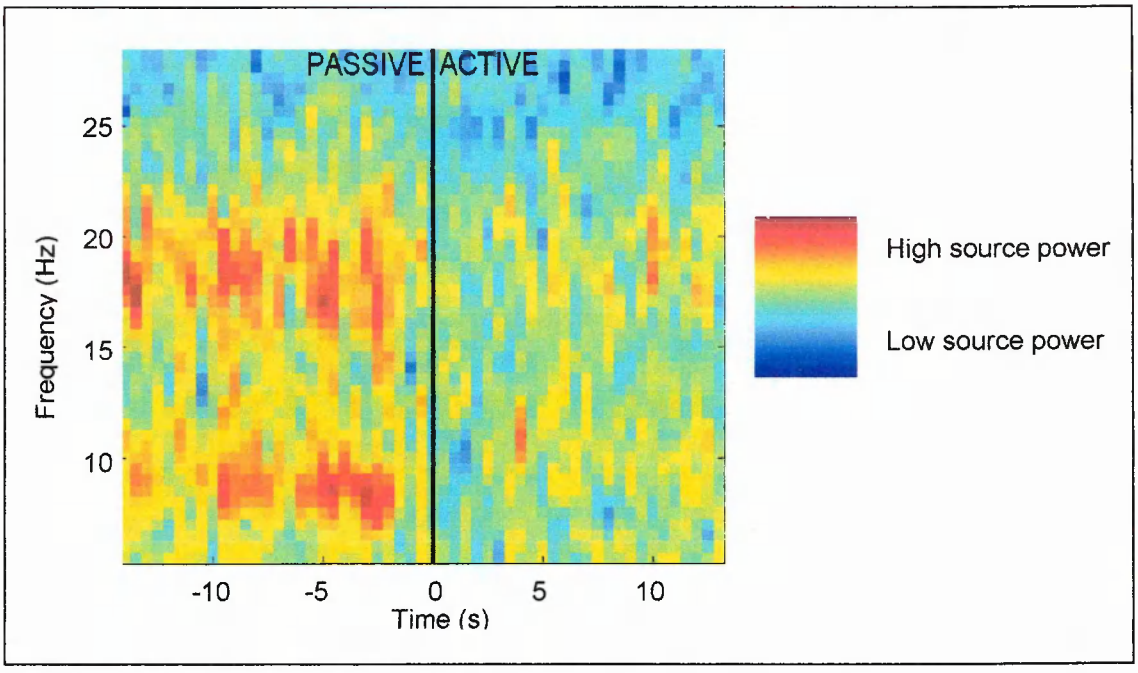


Figure 2.9, An example time-frequency representation showing a decrease in source power within low beta and alpha frequency bands during an "active phase" (Rippon, 2004, personal communication).

A windowed Fourier transform involves selecting a certain time window size, and sliding it along in time, computing the Fast Fourier Transform at each time using only the data within each window. However this may be problematic as there may be so few low frequency oscillations within a time window that frequency localisation is lost, and so many high frequency oscillations that time localisation is lost. Wavelet analysis has the advantage that it has a better time/frequency resolution.

2.8.5. Wavelet Analysis

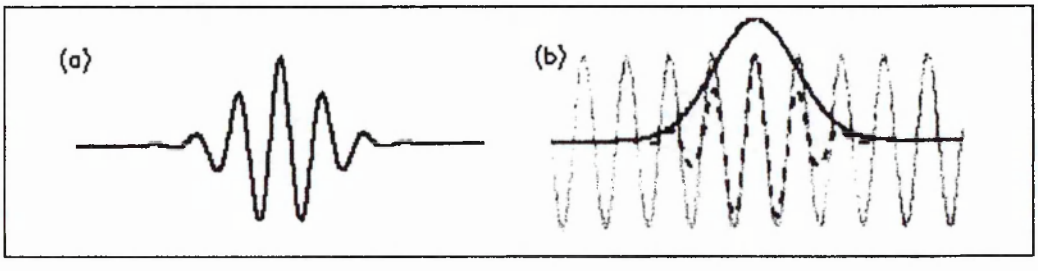


Figure 2.10. A Morlet wavelet (a) formed by multiplying a sine wave by a Gaussian envelope (b).

Figure 2.10 shows a Morlet wavelet. This is a sine wave multiplied by a Gaussian envelope. The wavelet has a finite duration and a specific frequency. By finding the correlation between the wavelet and each section of the time series it is possible to

determine a new time series of correlation against time. The width, or scale, of the wavelet can then be varied (this is defined as 1/frequency). Therefore, there is no problem associated with having more high frequency waves within a certain time window than low frequency waves, as the wavelet analysis always uses a wavelet of the same shape, it is just the size that is changed. By shifting the wavelet in time the signal is localised in time, and, by changing the scale, the signal is localised in terms of frequency. In this way a time-frequency representation can be produced.

Mann Whitney Analysis

The Mann Whitney (U) test can also be used in order to assess the statistical significance of these effects. By conducting wavelet analysis for each epoch in a dataset, values of source power can be obtained for different times and frequencies in both active and passive conditions or time periods. For each time / frequency point these source power values can be ranked in order to calculate the Mann Whitney (U) statistic (and corresponding Z score). In this way a time / frequency representation can be produced in which the Mann Witney statistic is represented by colour so that the time and frequency of any statisticall significant effects can be identified.

2.9, Summary

MEG is a non-invasive neuroimaging technique which directly measures neural activity with millisecond resolution. Using the beamformer technique, SAM, images of spectral power change (ERD/ERS) can be produced for predefined active and passive time windows. These images can be spatially normalised and averaged (Group SAM), and the statistical significance of these group effects assessed using SnPM. For virtual electrodes placed within regions of interest time-frequency representations can be produced using wavelet analysis. In this way the neural correlates associated with a certain task/stimulus condition can be investigated within the domains of space, time and frequency.

Chapter 3

Language research and the use of neuroimaging technology.

Rugg (1999) argues that there are two principle goals associated with the cognitive neuroscientific approach to a complex cognitive ability such as language. Firstly an understanding of the "identity and organisation of the elementary operations" that underlie language (page 15) and secondly an understanding of how these operations are instantiated. Rugg (1999) goes on to outline various ways in which these issues can be addressed. One such approach allows investigation of language processes within the brain, within the context of psycholinguistic findings. He argues that when knowledge about a particular cognitive operation is considered to be sufficiently advanced, based on the results of psycholinguistic research, an experimental manipulation can be employed to "isolate" this operation, and its neural substrate can be identified. This is the approach that has been adopted within this thesis in order to study two such operations, those of semantic and phonological processing.

This chapter consists of a brief review of the investigation into language processing in the brain, and the contribution that can be made by various functional-imaging techniques. The "dual route" to reading is also discussed, whereby a dissociation between semantic and phonological processing streams can be identified behaviourally. The dual route is a broad approach, within which the specific questions addressed in the experimental chapters of this thesis can be considered. These experimental chapters (5, 7 and 9) report experiments designed to investigate the neural correlates associated with semantic and phonological processing, using various approaches (including both task and stimulus manipulations), and different experimental designs.

3.1, Lesion studies

The classic model of the neural basis of language, based upon lesion and deficit observations made by Broca, Wernicke and Lichtheim within the nineteenth century, and revived by Geschwind (1965), has been described as having "informed research for almost 150 years" (Poeppel & Hickok, in press). Originally Broca's area (which is usually defined as encompassing BA44 and BA45), was believed to be associated with speech output, or language production, whereas Wernicke's area (the left posterior superior temporal cortex) was associated with language comprehension.

Since this model was proposed, there has been a great deal of evidence indicating that the neural basis of language is far more complex. Specifically, Poeppel & Hickok (in press) criticise the model in three ways. Firstly, whereas the classical model assumes that clinical syndromes are homogenous entities with a fixed set of syndromes, it is now appreciated that aphasic syndromes are comprised of variable clusters of syndromes, indicative of more fine-grained dissociations, and a much more complex system. Secondly, the model is criticised for relying upon a dramatically underspecified model of language, which ignores the many different representational systems identified through the behavioural studies discussed previously. Thirdly, the model is described as being "anatomically underspecified", as it fails to acknowledge the roles played by a number of other regions which have consistently been linked to language processing, such as the anterior superior temporal lobe, the middle temporal gyrus, and the temporo-parietal junction (Poeppel & Hickok, in press, page 5).

More recent models of language processing, which have also been derived using the lesion-deficit approach, have, for example, implicated the middle temporal gyrus as playing a role in word-level comprehension, the posterior superior temporal gyrus and inferior parietal cortex in auditory short-term memory, and anterior and inferior frontal gyrus in working memory functions (Dronkers, Redfern & Knight, 2000).

However, even when attempts are made to overcome problems brought about by functional and anatomical underspecification, there are a number of other problems associated with using data from lesion studies to inform an understanding of the neural basis of language processing. Many of these can be partially overcome by the use of functional imaging. For example, lesion studies tend to involve small, and possibly unrepresentative samples, whereas functional imaging techniques such as PET, fMRI, EEG and MEG allow the mapping of language processes in undamaged brains. They can also be used to investigate the function of brain regions that are rarely damaged, such as the insula (Rugg, 1999). Another way in which functional imaging can extend the approach taken by lesion studies is by enabling investigation into the dynamics of neural activity associated with a particular linguistic process. EEG and MEG allow investigation of the time course of such processes with millisecond accuracy. This allows research to move closer towards the goal of tracking language processes in both space and time.

3.2, Semantic / phonological processes

Language has been described in terms of the "activation, co-ordination, and integration of complex representational systems ... operating at millisecond speed" (Brown & Hagoort, 1999, page 4). More specifically, within the process of reading individual words, behavioural data has tended to differentiate between three main representational systems, relating to orthography, phonology and semantics (Gerhand, 2001; Ho, Chan, Lee, Tsang & Luan, 2004; Ellis & Young 1988).

The studies reported in this thesis involve the use of Magnetoencephalography to investigate particular issues relating to semantic and phonological processing. The "dual route" to reading, which differentiates between semantic and phonological processing streams (Ellis & Young, 1988), is of relevance to the interpretation of the results obtained within these studies.

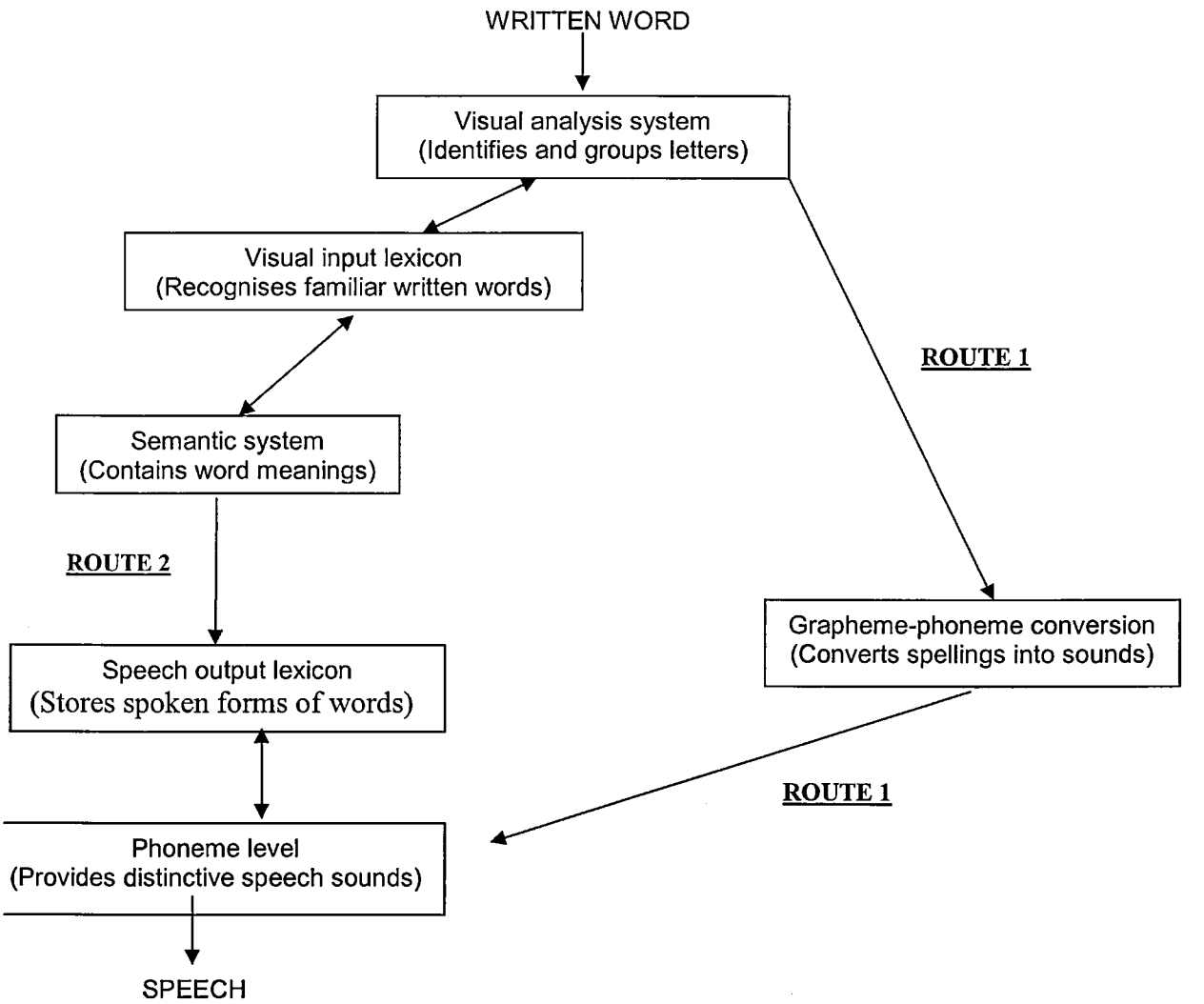
The dual route

Models of reading have described semantic and phonological forms of processing in a number of different ways. For example, Price (2000) describes them as "principle types of memory" necessary for effective language use (page 335), Plaut, McClelland, Seidenberg & Patterson (1996) describes a reading system that "incorporates a graded division of labour between semantic and phonological processes" (page 56), and Poldrack, Wagner, Prull, Desmond, Glover & Gabrieli (1999) describe them as "component linguistic functions" which themselves consist of separable processes (page 15).

This separation of semantic and phonological component processes seems to be supported by the findings of studies involving patients with acquired dyslexia (impairments of reading produced by brain damage). Based upon these findings, Ellis and Young (1988) described a model of reading that incorporates different "routes" which differentiate between semantic and phonological word processing (Figure 1). The first route has been termed "grapheme-phoneme conversion" and involves determining word pronunciation in a piecemeal fashion. Surface dyslexics have been reported to show impairment when reading irregular words (words that do not have regular spelling-sound correspondence), but less impairment when reading regular words. This was interpreted as showing a strong reliance upon reading route one.

Phonological dyslexics however show less impairment specific to regular or irregular words. Their impairment appears to be specific to unfamiliar words and nonwords. This supports the notion of a second route to reading which involves searching for words in a visual input lexicon and obtaining their meanings from the semantic system without reliance on the sound structure of the word.

Figure 3.1, The semantic and phonological routes for word reading as described within the Ellis and Young (1988) model, (the figure has been adapted from Ellis and Young (1988) to show only the first two reading routes.)



It has been argued that neurobiological data can provide evidence for the neural reality of these different representational systems (Brown & Hagoort, 1999). In order to investigate these streams using functional-imaging, the two reading routes must be isolated by experimental manipulation. There have tended to be two main approaches (as reflected by a metanalysis of neuroimaging studies reported by Jobard, Crivello & Tzourio-Mazoyer, 2003). Experiments have either involved the use of tasks designed to draw attention to the phonological or semantic nature of a stimulus, or the stimuli themselves

have been manipulated in order to facilitate, or inhibit, such processing. Each of these approaches will be considered.

3.3, Task manipulations

Within certain studies tasks designed to encourage participants to access the meaning of words have been contrasted with tasks believed to require participants to access the sound structure of a word. For example, "semantic tasks" have included tasks in which stimuli have to be matched according to their meaning, or the size of their referents (Vandenberghe, Price, Wise, Josephs & Frackowiak, 1996), other such tasks require participants to make decisions believed to require semantic processing, such as to decide whether a word refers to a living or a nonliving entity (Otten & Rugg, 2001; Kapur, Craik, Tulving, Wilson, Houle & Brown, 1994), whether the word is concrete or abstract (Wagner, Schacter, Rotte, Koutstaal, Maril, Dale, Rosen & Buckner, 1998; Poldrack, Wagner, Prull, Desmond, Glover & Gabrieli, 1999; Demb, Desmond, Wagner, Vaidya, Glover & Gabrieli, 1995), or whether a word belongs to a certain semantic category (Van Orden, Johnston & Hale, 1988). Tasks have also been used which require participants to make semantic decisions about the associations between words, for example to decide whether two words are synonymous (Roskies, Fiez, Balota, Raichle & Petersen, 2001), and which require participants to generate semantically associated words, such as verbs that may be associated with a given noun (Bucker, Corbetta, Schatz, Raichle & Petersen, 1996).

Phonological tasks have included those in which participants are required to count the number of syllables within a word (Mummery, Patterson, Hodges & Price, 1998; Otten & Rugg, 2001; Price, Moore, Humphreys & Wise, 1997; Poldrack et. al. 1999; Gabrieli, Poldrack & Desmond, 1998), make decisions about whether words rhyme (Roskies et. al. 2001), and generate rhymes in response to a given word (Sergent, Ohta, & Macdonald, 1992).

A methodological advantage associated with the use of such paradigms, is that as task manipulations are used to promote different types of processing, the same stimuli can be used within each task condition. This means that the effects of any confounds associated with the choice of stimuli may be reduced, provided that these confounds do not interact with different task conditions in different ways.

A potential problem with such studies involves the demands placed upon executive control processes. For example, when two different task conditions are randomly ascribed to different trials, it has been found that trials in which the participant has to switch task have been consistently associated with significantly longer reaction times (a "switch cost") compared to those that do not involve a task switch (Rogers & Monsell, 1995; Brass & Cramon, 2002; Mayr & Kliegl, 2003; Meiran, 1996). Within studies designed to investigate the neural correlates of semantic and phonological processing using different task conditions, this switch cost may serve to obscure the results, particularly those associated with the temporal dynamics of such processes.

3.4. Stimulus manipulations

Another approach has been to manipulate the stimuli in order to bias a certain type of processing. For example, as a result of a metanalysis, Jobard et. al. (2003) observed a number of ways in which stimulus manipulations have been used to dissociate between semantic and phonological processing. Firstly, a number of studies have used pseudowords, as these do not have a semantic representation, and are therefore believed to bias the phonological route. Such studies have compared conditions in which participants are required to read pseudowords and real words (Hagoort, Indefrey, Brown, Herzog, Steinmetz & Seitz, 1999; Price, Wise & Frackowiak, 1996), or to passively view both types of stimuli (Petersen, Fox, Snyder & Raichle, 1990).

Other such studies have involved the use of different word types, which are believed to afford different types of processing. For example, irregular words (such as "yacht") cannot be pronounced using only spelling-to-sound conversion rules, suggesting a strong reliance upon a lexical/semantic route. Similarly, in Japanese, whereas Kana writing refers to syllables that constitute words, Kanji writing corresponds to ideograms where a symbol globally refers to a meaning. These different types of writing system have therefore been used to dissociate between the two reading routes (Jobard et. al. 2003).

A potential problem associated with this methodology is that, by using different types of stimuli in different conditions, confounds may be introduced. For example, pseudowords and real words not only differ in terms of the type of processing they afford, it is also likely that they differ in terms of, for example, processing time and familiarity.

One study may have overcome such problems. Instead of manipulating the type of stimuli used within the two conditions, the nature of the associations between stimuli was manipulated. Participants were required to attend to the associations between words that either rhymed, or were semantically related (McDermott, Petersen, Watson & Ojemann, 2003). The use of such a paradigm is likely to have avoided the problems associated with using different word types within each of the two conditions. However, the task used within this study (i.e. to attend to the relations between words) does not appear to have been as stringent as those used within other studies. This may be a general drawback associated with the use of stimulus manipulations to promote phonological or semantic processing, rather than task manipulations. Within such studies it is difficult to control for the strategies that may be employed when processing the different types of stimuli.

Conversely, it may be that the use of stimulus manipulations provides a more stringent control as, for example, the use of nonword stimuli may prevent any use of a semantic route, and the use of irregular words preclude the possibility of phonological processing taking place. This approach may therefore prevent any implicit phonological processing within the semantic condition, and vice versa, in a way that cannot be achieved using task manipulations (as discussed in Chapter 4). However, it is not clear whether implicit processing is still possible, for example, the similarity between nonwords and certain real words may give rise to a certain degree of semantic analysis within the phonological task condition.

3.5, Imaging techniques and their contribution to language research

The choice of imaging technique has implications for the experimental design that can be employed, and the extent to which the results can inform the debate. The contribution that each of these functional imaging methods can make to the study of language processing will be briefly considered.

3.5.1, Haemodynamic methods

These methods rely on coupling between the net activity of a neuronal population and changes in its blood supply. Both fMRI and PET are techniques that measure the haemodynamic correlates of neural activity. There are a number of drawbacks associated with such techniques. Firstly, neither the physiological mechanism underlying the coupling between the blood supply and neural activity, nor its functional significance, are well

understood (Barinaga, 1997). Also, although changes associated with the timing of neuronal activity (i.e. asynchronous or synchronous firing) are likely to have functional significance, they are unlikely to affect the haemodynamic response (Kreiter & Singer, 1996).

PET

Within this method a short-lived isotope, usually $^{15}O_2$ in the case of "cognitive-activation" studies (Rugg, 1999), is introduced into the bloodstream, and accumulates in different brain regions in proportion to the amount of blood flowing in each region. The decay of this isotope gives rise to positron-electron annihilation events which can be detected outside the body. Three-dimensional images can be produced in which the intensity is proportional to the number of annihilation events, and therefore also proportional to the blood flow at that location, integrated across the acquisition interval (typically between 30 and 60s). The spatial resolution is approximately 5mm.

Cognitive studies, such as those designed to investigate language processes, involve the acquisition of such images from at least two experimental conditions, which are believed to differ only with respect to the cognitive operation under investigation. The two sets of images are then contrasted in order to identify regions in which regional cerebral blood flow (rCBF) differs. These results can be presented as statistical maps.

There are a number of drawbacks associated with using PET to investigate language processes. As the time interval needed for data acquisition is typically greater than 30s, temporal resolution is poor, and research can only be carried out using a "blocked design", whereby each scan is made over a succession of trials constituting a single experimental condition. Such a design introduces "state-related" differences that cannot be separated from time-locked "stimulus-related" differences. It has also been argued that such designs are prone to "condition-specific sets or strategies" which may modify stimulus-related effects (Rugg, 1999, page 20). Also, trials cannot be sorted in a post-hoc way, for example with respect to accurate/inaccurate responses. Another limitation associated with PET is the fact that a limited number of scans can be obtained from each participant. This restricts the number of conditions that can be used in a Within Subjects study, and makes it advantageous to pool data across subjects in order to achieve sufficient statistical power, which assumes that individual differences are small.

fMRI

Blood oxygenation level dependent (BOLD) imaging relies on the fact that the increase in blood supply, triggered by increases in neural activity, delivers more oxygen than is needed to meet the metabolic demand, and that the magnetic susceptibility of deoxyhaemogobin is greater than that of oxyhaemoglobin. Therefore an MRI signal sensitive to variations in susceptibility will reflect the ratio of deoxy- to oxy-haemoglobin, and also changes in local neural activity.

A typical acquisition time for an individual slice is 100ms, with a spatial resolution of approximately 3mm (Rugg, 1999). The "box-car" design is commonly used within fMRI studies. This involves the alternation of blocks of two or more experimental conditions throughout the data acquisition. However, as with PET experimental designs, this is subject to possible "state-related differences". However fMRI has the advantage that it does not involve the administration of ionising radiation, a procedure that restricts the number of observations that can be made from each participant. This means that there is more flexibility associated with the length of experimental blocks and the use of counterbalancing. Also, although the majority of fMRI studies have employed blocked experimental designs, it has been argued that event-related fMRI (employing a trial-by-trial experimental design) is possible, and a rapidly developing method (Rugg, 1999).

Such event-related techniques have the advantage of enabling investigation into the time course of stimulus processing. However, it has been argued that in the case of fMRI, responses are delayed and prolonged relative to the onset of the neural events that trigger them (Friston, Jezzard & Turner, 1994), although apparently reliable differences have been reported in latency and duration (as reviewed by Rugg, 1999, page 23). The temporal resolution of fMRI has been estimated as between 0.5s to 1s (Rugg, 1999).

3.5.2, Electrophysiological methods

Electrophysiological methods have the advantage that they measure neural activity directly. Such studies investigating cognitive function also tend to employ trial-by-trial designs, so that trials can be randomised and the neural processing of different classes of stimuli can be measured with a temporal resolution in the order of milliseconds. This time resolution is believed to be sufficient for tracking the neural correlates of cognitive processes in real time (Rugg, 1999), and especially necessary in the investigation of

language processing, where it is important to integrate spatial and temporal information (Brown & Hagoort, 1999).

3.6, Conclusion

Within this chapter language research and the application of neuroimaging techniques have been considered in general terms. Within the following chapters, certain issues relating to semantic and phonological language processes are discussed in more detail, and studies reported in which the neuroimaging technique Magnetoencephalography was used to investigate these issues.

In summary, in order to investigate the neural correlates of semantic and phonological processing, two main approaches have been adopted. Studies have either involved the use of task manipulations, or stimulus manipulations. Each approach is associated with methodological drawbacks. Within this thesis both approaches have been adopted. Chapter 5 describes a study that involved the use of task manipulations in order to investigate the neural correlates of semantic and phonological processing, whereas Chapter 9 describes a study that involved the use of stimulus manipulations. Within the study outlined in chapter 7, a new approach was adopted whereby task cues were used to prime semantic and phonological processing routes (or "task sets"), so that their neural correlates could be investigated in the absence of confounds associated with the choice of stimulus.

Chapter 4

The neural correlates of semantic and phonological processing.

4.1, Overview

Neuroimaging studies have revealed differential effects within the brain that appear to be associated with semantic and phonological task conditions (Abdullaev & Posner, 1998; Roskies et. al. 2001). By asking participants to engage in tasks designed to draw their attention to either the meaning or the sound structure of visually presented words, distributed networks of brain regions have been described for both semantic and phonological processing. A selection of these results is presented in Appendices 4.1-4.14, and show the regions that have been associated with task dependent differential effects. As these tables show, semantic networks have tended to include left temporal/temporo-parietal cortex, left anterior inferior parietal cortex, right cerebellum and anterior cingulate (Posner, Abdullaev, McCandliss & Sereno, 1999; Vandenberghe et. al. 1996; Noppeney & Price, 2003; Roskies et. al. 2001) whereas phonological networks have tended to consist of parietal regions including the supramarginal gyrus (Mummery et. al. 1998), the temporo-parietal junction (Petersen, Fox, Posner, Mintun & Raichle, 1989), the left superior temporal lobe (Posner et. al. 1999) and Broca's area (Paulesu, Frith & Frackowiak, 1993). The involvement of each of these regions will be considered, together with findings associated with the time course of task specific effects, and suggestions regarding the nature of interactions between the different regions.

4.2, Semantic networks

4.2.1, Semantic processing and middle temporal and left posterior temporo-parietal regions.

Lesion studies

Lesions within temporal and temporo-parietal regions have suggested their involvement in semantic processing. For example, patients with "transcortical sensory aphasia" have been reported to show a severe comprehension deficit despite speech and repetition being intact. These patients have lesions distributed within the left inferior-temporal lobe, and the posterior inferior-parietal lobe (at the junction of Brodmann's areas 39 and 19) (Alexander, Hiltbrunner & Fischer, 1989).

Similarly, patients with "semantic dementia" show a gradual loss of word retrieval and word comprehension, which has been associated with atrophic changes in the temporal lobes, specifically in the left hemisphere (Hodges, Patterson, Oxbury & Funnell, 1992). Rather than showing impairment specific to linguistic tasks, it has been reported that these patients also show a semantic impairment on non-verbal tasks, with other cognitive functions being relatively spared (Schwartz, Marin & Saffran, 1979). These findings suggest that the temporal lobes may play a role that is associated with semantic processing in general, rather than being specifically linked to verbal semantics.

Neuroimaging studies

Neuroimaging studies seem to confirm a left inferior temporal involvement in semantic processing. Such studies have compared semantic tasks such as naming and matching words according to the colour and location of their referents, to nonsemantic tasks such as responding to visual controls and matching words according to the number of syllables (Price, 2000, Mummery et. al. 1998).

This temporal lobe specificity for semantic task conditions does not seem to be limited to the processing of visually presented words. Differential effects within the left middle and inferior temporal gyri and left superior temporal regions have been reported from PET studies that have compared the monitoring of auditory concrete nouns according to semantic criteria with the monitoring of pure tones according to their pitch (Démonet, Chollet, Ramsay, Cardebat, Nespoulous, Wise, Rascol & Frackowiak, 1992).

In support of the findings from lesion studies, PET findings suggest that the left inferior temporal gyrus (specifically BA20), and BA21 within the left middle temporal gyrus may form part of a distributed semantic processing network common to both words and pictures (Vandenberghe et. al. 1996, Bookheimer, Zeffiro, Blaxton, Gaillard & Theodore, 1995). Within the PET study reported by Vandenberghe et. al. (1996) two semantic tasks (matching for meaning and matching for real-life size) were compared to a low-level baseline task (matching according to physical stimulus size) using both word and picture stimuli. Regions of overlap were identified in which significant activation was observed in both of the semantic conditions compared to the baseline for both words and pictures ($p<0.01$). In this way a distributed semantic system shared by words and pictures was established. Besides BA20 and BA21 in the left inferior and middle temporal cortex, this system also included regions within the left fusiform gyrus (BA21/37), the left parieto-

temporal junction, the right cerebellum and left inferior frontal regions, each of which will be considered in the following sections.

There have also been suggestions that left inferior temporal cortices may be involved in the processing of semantically meaningful items, even in the absence of a specific task to direct attention to it's semantic nature. For example a PET study showed the middle temporal gyri to be activated to a greater extent during real word reading than during pseudoword reading (Hagoort et. al. 1999). This has been interpreted as showing a greater left inferior temporal involvement in the processing of semantically meaningful stimuli, which may be indicative of implicit semantic processing (Turkeltaub, Eden, Jones & Zeffiro, 2002).

Left posterior temporo-parietal regions (including the angular gyrus)

Lesions within the posterior inferior-parietal lobe (at the junction of Brodmann's areas 39 and 19) have also been identified in patients with transcortical sensory aphasia (Alexander, Hiltbrunner & Fischer, 1989). The angular gyrus within BA39 was originally linked to a "visual word form system" (Price, 2000). Bilateral activation within the temporo-parietal junction has been observed using PET when participants silently read as opposed to when they rested with their eyes closed (Price, Moore & Frackowiak 1996). Although one interpretation of these findings is that the region may be generally involved with lexical processing, it also possible, based upon the previous discussion regarding the inferior temporal region, that implicit semantic processing may have lead to these results. Other silent reading studies have not shown angular gyrus involvement (Brunswick, McCroy, Price, Frith, & Frith, 1999), possibly due to reduced implicit semantic processing.

In keeping with this interpretation, it has more recently been claimed that the angular gyrus forms part of a distributed semantic system (Price, 2000). This has been supported by studies in which the level of semantic processing of visually presented words has been controlled by task conditions. For example, Mummery et. al. (1998) reported enhanced PET activation within the left temporo-occipital-parietal junction (BA39) when participants were required to make decisions based upon the semantic associations of visually presented words as opposed to the number of syllables. As with the semantically related temporal regions, the left inferior parietal region seems to show specificity for the processing of semantically meaningful stimuli, irrespective of whether they are presented

visually or phonologically (Démonet et. al. 1992), or whether they are presented as words or pictures (Vandenberghe et. al. 1996).

Task difficulty as a possible confound

A number of the studies that have reported an enhanced left temporal response for semantic tasks compared to non-semantic tasks have also reported larger reaction times for the semantic condition (Vandenberghe et. al. 1996). If reaction time is taken as a measure of task difficulty, it may be that the inferior temporal response reflects the difficulty of a task rather than it's semantic nature. Using PET, Mummery et. al. (1998) investigated two semantic tasks in which participants were required to match visually presented nouns in terms of the colour with which their referents are associated, and the location in which they are found. These semantic tasks were compared with a nonsemantic syllable counting task. Behavioural results show that the syllable task produced significantly longer reaction times than both of the semantic conditions ($p<0.0001$). Despite these behavioural findings, the PET results revealed significantly stronger activation for the semantic tasks compared to the syllable task within the left inferior temporal gyrus, the left middle temporal gyrus and the left temporo-occipito-parietal junction (BA39), suggesting that this response is associated with the semantic nature of the task rather than task difficulty.

Semantic / phonological comparisons

The syllable counting task used within the study reported by Mummery et. al. (1998) is thought to require phonological processing (processing of the sound structure of the stimulus). The findings indicate that the left inferior temporal and middle temporal responses differentiate between semantic and phonological processing. Other studies appear to have replicated these findings using a variety of tasks (McDermott, Petersen, Watson & Ojemann, 2003, Démonet et. al. 1992). Left superior/middle temporal (BA22/21) differential effects have even emerged when participants were not required to make an overt response, but were asked to "attend closely to the relations between words" in lists of either semantically associated words, or words that rhyme (McDermott et. al. 2003).

A possible semantic role for the temporal and temporo-parietal regions

Based upon the apparent semantic specificity of these temporal and temporo-parietal regions (specifically BA20 and BA39), and in keeping with the model proposed by Ellis & Young (1988), it has been suggested that these regions may form part of a "semantic route to reading" (Price, 2000, page 348). Other authors agree with this assumption, although descriptions have varied, for example these regions have also been described as "correlates of stored semantic knowledge" (Price, Indefrey & Turennout, 1999, page 231), and a "concept centre" (Price, 2000, page 355). Support for such conclusions has come from reports of category-specific differential effects within these cortical areas.

Category differences

Category-specific differential effects have been associated with the inferior temporal gyrus, for example an enhanced inferior temporal response for animals relative to artefacts when these stimuli are presented as pictures (Perani, Cappa, Bettinardi, Bressi, Gorno-Tempini, Matarrese, & Fazio, 1995), and as visually presented nouns (Pulvermüller, 2001). More extensive left BA20 activation has been associated with the processing of concrete as opposed to abstract words (Beauregard, Chertkow, Bub, Murtha, Dixon & Evans, 1997). There are also reports of patients with bilateral inferomedial temporal lobe damage who show impaired performance on specific categories, such as living things relative to artefacts (Funnell & Davies, 1996). Although it has been suggested that variables such as familiarity may account for such dissociations, it seems more likely that differences in the type of semantic associations bring about these differential effects (Mummery et. al. 1998). For example, items from categories such as living things and concrete nouns are likely to be distinguished primarily by their perceptual (mainly visual) features, whereas artefacts and tools may be more strongly specified by their functional attributes.

In an event-related potential study in which the processing of nouns and verbs was compared using a lexical decision task (Pulvermüller, Lutzenberger, & Preissl, 1999), strong category differences were observed above motor and visual cortices. These findings coincided with a dissociation between behavioural data regarding the semantic associations of the word groups (visual or motor). Support for this approach has been provided by studies that have shown selective left premotor responses to "high action" words such as

tools (Martin, Wiggs, Ungerleider & Haxby, 1996; Grafton, Fadiga, Arbilo & Rizzolatti, 1997), patients with left frontal/parietal lesions showing impairment with verbs, and patients with left temporal lesions showing impairment with nouns (Daniele, Giustolisi, Silveri, Colosimo & Gainotti, 1994; Gainotti, Silveri, Daniele & Giustolisi, 1995). There have even been reports of differential neural responses to verbs depending upon the part of the body with which they are associated (Hauk, Pulvermüller & Johnsrude, 2003).

It has been noted that the inferior temporal cortex is "the terminus of the "what" or object recognition stream" in vision, lying in close proximity to limbic structures that receive converging input from all sensory systems (Saffran & Sholl, 1999, page 257.) It is therefore plausible that the inferior temporal response reflects the extent to which sensory associations are made, and this may explain the reports of a preferential inferior temporal response for concrete nouns compared to abstract nouns, nouns compared to verbs, and living things compared to artefacts.

Vandenberghe et. al. (1996) adopted this approach by noting that in monkeys the inferior temporal cortex and ventral frontal convexity are known to be involved in object recognition, and suggesting that "when primates acquired language a pre-existing object-recognition system could have been adapted to attribute meaning to nouns" (page 255). This is compatible with the idea of "correlational learning", described by Pulvermüller (2001), whereby, on the basis of experience, networks or "word webs" are established within temporal regions which reflect aspects of a words referential meaning.

Although more research is needed to clarify the nature of these processes and the precise role of these temporal regions in semantic processing, it has been argued that it is not surprising that there should be some relationship between perception and conceptualisation as perceptual characteristics are essential components of meaning (Saffran & Sholl, 1999). Regardless of the way such information is represented, these findings further support the notion that temporal and temporo-parietal regions play an important role in semantic processing, and may in some way be associated with the storage of information regarding semantic attributes.

Medial temporal regions (including the fusiform gyrus, parahippocampal region and the hippocampus)

More inferior / medial temporal regions, including the fusiform gyrus, and parahippocampal regions have also been implicated in descriptions of semantic networks. Various studies, for example, comparing semantic with low level tasks, such as animacy decisions compared to syllable decisions (Otten & Rugg, 2001), abstract/concrete decisions compared to uppercase/lowercase decisions (Wagner, Schacter, Rotte, Koutstaal, Maril, Dale, Rosen & Buckner, 1998), and tasks comparing the processing of semantically related and phonologically related stimuli (McDermott et. al. 2003) have resulted in differential effects within the fusiform gyrus and parahippocampal region (BA37). The adjoining hippocampal region (BA36) has also been implicated by a study in which a semantic (synonym) task was compared with a phonological (rhyming) task (Roskies et. al. 2001). The fusiform gyrus has also been identified as a source of the N400, an evoked response component associated with semantic processing (McCarthy, Nobre, Bentin & Spencer, 1995). Such findings have lead to the suggestion that the left posterior inferior temporal gyrus, including the fusiform gyrus, may "mediate between the conceptual and the word form level" (Noppeney & Price, 2003).

Other studies have failed to find significant fusiform effects associated with semantic processing tasks (Kapur et. al. 1994). Roskies et. al. (2001) reported that a region of the fusiform gyrus (BA37) was active for both semantic and nonsemantic task conditions. Although the authors suggest that this may reflect a basal level of semantic processing present in each condition, an alternative explanation may be that this region plays a role that is specific to word processing rather than semantic processing. Desmond, Gabrieli & Glover (1998) suggest that it may be involved in the visual inspection of words, based upon the finding that a stem completion task using stimuli with relatively few possible completions resulted in significantly greater bilateral fusiform activation than when stimuli with many possible completions were used. However, Price & Friston (1997) have reported that the left posterior temporal lobe (BA37) seems to play a role common to reading, picture naming, letter naming and colour naming, when articulation is controlled for, suggesting that its role is not limited to visual inspection.

There have also been claims that this region may be more active during word generation than during semantic judgments on heard words, suggesting a possible role in lexical retrieval (Warburton, Wise, Price, Weiller, Hadar, Ramsay, & Frackowiak, 1996). It

is possible, however, that the nature of the semantic processing required for word generation tasks may differ from that required for other semantic judgements, and that this may account for differences in the fusiform response. It has been suggested, for example, that the middle fusiform region may be linked specifically to visual attributes of semantic memory. This approach has been challenged by authors who argue that this cannot be the case as the same area is activated when congenitally blind participants read words with abstract meanings using Braille (Price, 2000). However, it is possible that functional specificity develops differently in the absence of visual input making it difficult to draw conclusions based upon these findings.

Although it seems that there is an increasing consensus that the posterior temporal cortex (the left fusiform gyrus and parahippocampal gyrus) plays a role that is specific to semantic processing, the nature of this role is unclear. Left inferior and middle temporal regions appear to be much more consistently associated with semantic tasks. However, despite the strong evidence to suggest that the temporal cortex plays a crucial role in semantic processing, it has been claimed that it is the left inferior frontal cortex that responds most strongly to semantic task demands (Price et. al. 1999, page 231). In a study reported by Roskies et. al. (2001) participants were required to complete a synonym task (in which they decided whether two words had the same meaning) and a rhyme task. The middle temporal gyrus, and a region of the fusiform gyrus were active across both task conditions, and failed to differentiate between the semantic and phonological tasks. It may be the case that implicit semantic processing within the phonological task could have accounted for the lack of semantic/nonsemantic task differentiation within the temporal lobes. It has also been suggested that semantic systems within the temporal lobes may be so widely distributed that the diffuse activity remains below threshold (Roskies et. al. (2001). However, other regions, including those within the left frontal cortex did show differential effects between the synonym and rhyme task conditions within this study.

4.2.2, Semantic processing and left frontal cortex

There is strong evidence to support the results of Roskies et. al. (2001), and suggest that a distributed semantic system includes left prefrontal regions. Petersen, Fox, Posner, Mintun & Raichle (1988) were the first to suggest the involvement of left frontal regions in the semantic processing of words. Since then there have been reports of left lateral frontal lesions apparently affecting word processing tasks that require meaning analysis, such as

generating verbs associated with nouns, generating nouns associated with verbs, generating synonyms and selecting opposites (Bucker et. al. 1996).

Neuroimaging studies such as PET and fMRI have also reported enhanced left frontal activation within BA44, 45, 46 and 47 when participants are required to make living/nonliving decisions compared to detecting the letter "a" (Kapur et. al. 1994), and when participants make decisions about whether nouns are abstract or concrete compared to decisions about whether they are uppercase or lowercase (Wagner et. al. 1998, Demb, Desmond, Wagner, Vaidya, Glover & Gabrieli, 1995), or whether the first and last letters are in alphabetical order (Demb et. al. 1995).

Although Wagner et. al. (1998) reported bilateral inferior frontal differential effects when reading was compared to fixation, but left lateralised differential effects when a semantic task (abstract/concrete decision) was compared to a non-semantic task (case judgement), there have been reports which suggest that task dependent inferior frontal effects may not be specific to the left hemisphere. In a study which examined differential effects associated with making abstract/concrete decisions compared to case judgements, Poldrack, Wagner, Prull, Desmond, Glover & Gabrieli (1999) reported that besides significant effects within the left inferior prefrontal cortex (BA44, 45 and 47), six out of eight participants also showed significant effects within the right inferior prefrontal cortex.

One fMRI study addressed this lateralisation issue by investigating the neural correlates of semantic (abstract/concrete) and perceptual (uppercase/lowercase) judgements in patients who had undergone Wada testing for pre-surgical evaluation (Desmond, Sum, Wagner, Demb, Shear, Glover, Gabrieli & Morrell, 1995). Four patients had been found to be left-hemisphere dominant, and three were right hemisphere dominant for language. As predicted, regions within BA45, 46, and 47 showed significant increases in activation during semantic relative to perceptual judgements. Lateralisation of these increases was consistent with the Wada test assessments of hemispheric language dominance in each of the seven participants. It seems likely that this may account for the prevalence in reports of left lateralised inferior frontal effects.

BA10, 11, 8 and 9

Besides effects within BA 44, 45, and 47, more anterior differential effects have also been reported which appear to show specificity for semantic tasks as opposed to

nonsemantic tasks, for example within left BA10 (Kapur et. al. 1994, Roskies et. al. 2001; Demb et. al. 1995), right BA10 (MacLeod, Buckner, Miezin, Petersen & Raichle, 1998), left BA11 (Vandenberghe et. al. 1996) and more superiorly in left BA8 and 9 (Roskies et. al. 2001, Demb et. al. 1995) and right BA9 (MacLeod, Buckner, Miezin, Petersen & Raichle, 1998). The possible role of these regions will be discussed later in the chapter, the role of left inferior frontal regions including BA 44, 45 and 47 will be considered first.

Differential effects within BA 45, 46 and 47.

Evidence suggests that the differential effects observed within BA45, 46 and 47 might not be specific to linguistic stimuli. Vandenberghe et. al. (1996) have reported enhanced inferior frontal activation when participants matched stimuli according to meaning and real-life size compared to physical stimulus size, irrespective of whether the stimuli were words or pictures. It also appears that the effect is not specific to the semantic processing of visually presented stimuli. Petersen et. al. (1989, page 160) reported "good overlap" of semantic inferior prefrontal effects across visual and auditory presentation modalities. Noppeney & Price (2003) also reported significant left inferior frontal effects specifically for semantic tasks when participants were presented with auditory stimuli. It has even been argued that implicit semantic processing involved with the passive viewing of real words as opposed to pseudowords is enough to produce enhanced levels of activation within the left inferior frontal cortex (Petersen, Fox, Snyder & Raichle, 1990).

Based upon a review of the literature, Gabrieli, Poldrack & Desmond (1998) claimed that left prefrontal activation reflects "psychological processes that are involved in semantic analyses across many tasks, that operate across verbal, pictorial, visual, and auditory modalities, and that are engaged both intentionally and incidentally" (page 907). These findings support the original claim that this region (specifically BA45, 46 and 47) represents the site of semantic networks and is involved specifically in semantic processing, as opposed to non-semantic forms of processing (Petersen et. al. 1988).

However, the studies discussed that have reported task dependent left inferior frontal differential effects have tended to involve comparisons between semantic tasks and low-level tasks such as case judgement (Wagner et. al. 1998; Poldrack et. al. 1999; Desmond et. al. 1995; Demb et. al. 1995), letter detection (Kapur et. al. 1994) and alphabetical decisions (Demb et. al. 1995). It seems likely that low-level tasks such as these would tend to involve orthographic analysis of the stimuli. It has been argued that

when semantic processing is compared to phonological processing (analysis of the sound structure of a word), left inferior frontal differences have either not been reported, or are limited to a small region of BA47 and the medial superior-frontal cortex (Price et. al. 1999).

Semantic processing compared to phonological processing and the left inferior frontal cortex: Reports of semantic and phonological processing involving the same left inferior frontal regions.

It has been reported that relative to low level baseline tasks (for example fixating on a crosshair), tasks which draw attention to semantic and phonological relations between words elicit activation in many of the same frontal regions, including left inferior frontal cortex (BA45/46 and BA44/45/46), the right inferior frontal cortex (BA44/45), and the medial frontal gyrus (BA6) (McDermott et. al. 2003). Although these authors also report differences within the semantic / phonological comparison, there are other studies in which significant differences between semantic and phonological processing have failed to emerge (Price, Moore, Humphreys & Wise, 1997). As a range of tasks have been used to investigate semantic and phonological processing, it is possible that intervening variables, may account for the discrepancy between these findings. One such variable might be task difficulty.

Task difficulty

It seems likely that semantic and phonological decisions would tend to be more difficult than other low-level, orthographic decisions. If it can be assumed that the time taken to complete a task is indicative of task difficulty, then behavioural evidence suggests that this is the case (Kapur et. al. 1994). Poldrack et. al. (1999), for example, report a tendency for case judgements to be completed faster than semantic and phonological tasks, and no significant difference between the time taken to complete semantic and phonological tasks. Based upon these findings, it seems possible that the variable of task difficulty influences the left prefrontal response, especially as research indicates that frontal activity can be modulated by the difficulty of a semantic judgment, (as reflected by differences in reaction time and accuracy scores) (Roskies et. al. 2001).

In order to investigate the effect of task difficulty, Demb et. al. (1995) presented participants with three tasks that had first been tested behaviourally. Encoding task

latencies were assumed to reflect task difficulty. Two non-semantic tasks involving uppercase/lowercase decisions, and decisions about whether the first and last letters were in alphabetical order, were compared to a semantic task of deciding whether the word was abstract or concrete. Reaction time data indicated that the alphabetic task took longer to complete than the semantic task, and participants were generally quickest when performing the uppercase/lowercase task. Despite these reaction time differences, recognition memory performance significantly differed across encoding conditions ($p<0.0001$) with greater recognition for semantically encoded words, as would be expected from the level of processing effect. Similarly, enhanced left inferior frontal activation was observed for the semantic task conditions, irrespective of differences in reaction time, suggesting that differences in task difficulty can not fully account for task dependent left inferior frontal differences, or the apparent absence of left inferior frontal differences for certain semantic/phonological comparisons.

Implicit semantic processing

It has been argued that reports of similar left inferior frontal activation patterns for semantic and phonological tasks do not exclude the role of the frontal lobes in semantic processing, as regions showing no significant differences could have been involved with implicit semantic processing in phonological task conditions, or implicit phonological processing in semantic task conditions (Price et. al. 1999).

It has been proposed that words that are processed to the level of phonology are automatically processed semantically (Poldrack et. al. 1999). Behavioural evidence seems to support this theory, for example, Gabrieli et. al. (1998) compared the reaction time results for a phonological task involving syllable counting using real words, and using nonwords. Participants typically made phonological decisions about real words within 830ms, and phonological decisions about nonwords within 900ms. The authors interpret this difference as illustrating that the semantic status of real words influenced the phonological decisions. However, other possible confounds are not considered, such as differences in familiarity and the lexical status of words and nonwords.

Even tasks comparing the processing of words with the processing of nonwords may not be immune to the effects of implicit semantic processing in the non-semantic condition. Although the use of nonwords seemingly prevents implicit semantic processing, it has been argued that when deciding how to pronounce nonwords, participants are likely

to draw upon their knowledge of similar real words, which could introduce a semantic element (Gabrieli et. al. 1998).

Implicit phonological processing

Similarly behavioural findings suggest that implicit phonological processing may occur during the completion of semantic tasks. For example, Van Orden et. al. (1988) reported phonologically driven false alarms in a category decision task, such as accepting "rows" as a flower, suggesting that phonological information automatically influenced performance of the semantic task. It has been suggested that the extent to which automatic phonological processing occurs may depend upon other possible confounding variables, such as the level of reading skill and the type of words read (Price et. al. 1999).

It seems reasonable to assume that if implicit phonological processing does occur within a semantic task, then this may influence the left inferior frontal effects observed as various lesion and neuroimaging finding have associated phonological processing with left frontal regions (Fiez & Petersen, 1998).

4.2.3, Phonological processing and the left inferior frontal cortex

Although it has been argued that lesion studies have provided evidence that processing phonological information may be selectively impaired, it has also been argued that the locations of lesions underlying these impairments have not provided a clear pattern (Burton, 2001). Lesions within the left inferior frontal cortex have resulted in difficulties with speech production that have implicated this region in articulatory and phonological processing (Poldrack et. al. 1999). However, lesions that are confined to Broca's area have tended to be associated with only motor deficits, larger lesions within this area (including regions of BA44 and 45) have resulted in damage to language processes typically associated with Broca's aphasia, such as non-fluent speech production, impaired sentence repetition and relatively preserved speech comprehension (Mohr, Pessin, Finkelstein, Funkenstein, Duncan & Davies, 1978).

The results of lesion studies with patients with phonological dyslexia have been interpreted in vastly different ways. In response to a review of the literature on phonological dyslexia conducted by Fiez & Petersen (1998), it has been claimed that as six out of seven patients with confirmed damage to the left frontal region exhibited deficits in

reading nonwords, this provides "preliminary evidence in favour for a role of the left frontal cortex in phonological processing" (Poldrack et. al. 1999). However, in response to the same review, Burton (2001) argued that as only three out of thirty-two cases of phonological dyslexia were associated with lesions contained exclusively within the frontal lobe, this fails to provide a consistent association. The authors themselves interpret these findings as "providing tentative support for a connection between left frontal lobe damage and phonological dyslexia" (Fiez & Petersen, 1998, page 918). As seven of the participants with phonological dyslexia had lesions limited to parietal, temporal and/or occipital cortices, the authors suggest that different subtypes of phonological dyslexia may account for these differences.

Neuroimaging studies

Neuroimaging studies seem to support the notion that left frontal and parietal regions are involved in different aspects of phonological processing. Using PET, Paulesu et. al. (1993) claimed to have identified the neural correlates of two subprocesses of verbal short term memory, or the "articulatory loop". They claim that their neuroimaging findings differentiate between a "subvocal rehearsal system" (which was believed to be utilised during both a rhyming judgement task and a task requiring letter strings to be remembered) and a phonological store (thought to be necessary for the memory task but not the rhyming task). Both of these tasks were compared to a control condition in which Korean letters were displayed, which could not be phonologically processed. When the results of the two phonological tasks were combined and compared to the control condition, significant activation was observed bilaterally within BA44, superior temporal gyri (BA22/42), supramarginal gyrus (BA40) and insulae. Following a comparison between the two task conditions, the authors conclude that while the supramarginal gyrus (BA40) appears to be involved in the short term memory task, but not the rhyming task, superior temporal regions and BA44 appear to be involved with phonological processing independent of memory, and therefore these regions were associated with a subvocal rehearsal system. The involvement of temporal and parietal regions in phonological processing will be discussed later in the chapter.

A left inferior frontal involvement in the phonological processing associated with letter rhyming has also been reported using fMRI (Temple et. al. 2001). Likewise, other phonological tasks have produced left inferior frontal effects, for example word rhyming tasks (Sergent, Ohta, & Macdonald, 1992), phoneme monitoring (Zatorre, Meyer, Gjedde

& Evans, 1996), and other phonological tasks, irrespective of whether the stimuli were presented visually or in auditory form (Gabrieli et. al. 1998). Following a review of various studies that have employed nonword and letter rhyming tasks, Burton (2001) reported that the predominant interpretation is that the inferior frontal gyrus can be "attributed to phonological rehearsal processes that are used to maintain verbal information for short periods of time" (page 699).

Nonword reading and the inferior frontal cortex.

In direct contrast to the results reported by Petersen et. al. 1990, which indicate that the passive viewing of real words elicits enhanced left inferior frontal activation compared to the passive viewing of pseudowords, other studies have reported preferential left inferior frontal activation during pseudoword reading compared to reading real words (Hagoort et. al. 1999; Price, Wise & Frackowiak, 1996). Although it is unclear why there is such a discrepancy between the two sets of results, those presented by Hagoot et. al. (1999) and Price, Wise & Frackowiak (1996) provide more evidence to suggest that phonological processing may be associated with left inferior frontal regions. These results have been interpreted as indicating that the left inferior frontal regions may play a role in spelling-sound conversion rather than being limited to sub-vocal rehearsal (Burton, 2001).

This interpretation also appears to be supported by the finding of greater inferior frontal activation in English readers when compared to Italian readers (Paulesu, McCrory, Fazio, Menoncello, Brunswick, Cappa, Cotelli, Cossu, Corte, Lorusso, Pesenti, Gallagher, Perani, Price, Frith & Frith, 2000). English and Italian differ in orthographic-phonological consistency, suggesting that the increased inferior frontal activation for English may be associated with a more complicated orthographic-phonological mapping. Even within the English language, differences in spelling-sound consistency ("regularity") and word length in a lexical decision task have been found to modulate the amount of right inferior frontal activation during phonological processing (Pugh, Shaywitz, Shaywitz, Shankweiler, Katz, Fletcher, Skudlarski, Fulbright, Constable, Bronen, Lacadie & Gore, 1997).

Therefore, when compared to low level tasks, both semantic and phonological processing have been strongly associated with inferior frontal effects. The question then emerges of whether and how these effects differ.

4.2.4, Separate left frontal regions for semantic and phonological processing

It has been argued that when semantic processing is compared to phonological processing differential effects may be limited to a small region of BA47 and the medial superior-frontal cortex (Price et. al. 1999). For example, Roskies et. al. (2001) compared tasks that required participants to determine whether pairs of words were synonyms or whether they rhymed. Three regions within the left inferior frontal cortex were identified as showing task dependent differential effects. Each of these regions were at, or near, BA47. The authors suggest that the discrepancy between these findings and others in which significant differences failed to emerge may arise from the nature of the semantic tasks. They argue that the semantic demands of their synonym task were greater than those of other tasks, such as tasks requiring a living/nonliving decision.

A number of authors have suggested that phonological and semantic tasks may recruit different subregions of the inferior frontal cortex (Roskies et. al. 2001; Fiez, 1997; Gabrieli et. al. 1998), and neuroimaging findings appear to support this notion. Several studies have identified a dissociation between anterior/ventral inferior frontal (BA47) effects, which have been linked to semantic tasks, and posterior/dorsal inferior frontal effects (BA44/45/6) which have tended to be associated with phonological tasks. For example, this dissociation has been reported from fMRI studies in which participants were required to attend to the relations between lists of words that either rhymed, or were semantically related to each other (McDermott et. al. 2003), make living/nonliving decisions compared to counting the number of syllables (Otten & Rugg, 2001; Price et. al. 1997), and make abstract/concrete decisions compared to counting the number of syllables (Gabrieli et. al. 1998).

Other studies have revealed a specificity of BA47 for semantic task effects compared to phonological tasks, but failed to show inferior frontal effects that are specific to phonological tasks. For example, Poldrack et. al. (1999) used fMRI to compare the neural correlates of a semantic task (abstract/concrete decision) and a phonological task (syllable counting). The results indicated that the anterior/ventral extent of the left inferior prefrontal gyrus was more active during semantic than phonological processing, whereas a more posterior/dorsal region was active in relation to both semantic and phonological processing. There was no evidence of greater activation in the left inferior frontal gyrus for phonological relative to semantic processing, which may be indicative of implicit

phonological processing in the semantic task condition.

Similarly, using PET, Mummery et. al. 1998 identified significant activation within BA47 for a semantic task (matching words according to the perceptual or associative attributes of their referents) compared to a phonological task (matching words according to the number of syllables), but no significant inferior frontal effects that were specific to the phonological task. This study also revealed significant effects within BA10/11 that were specific to the semantic task, a finding that has been supported by other studies (McDermott et. al. 2003). It therefore appears that the differential effects within BA47 and BA10/11 linked to semantic processing are the most robust. Despite this, it has been claimed that the role of such regions in semantic processing has "remained elusive" (Burton, 2001, page 695).

4.2.5, The role of left inferior frontal regions in semantic processing

Originally left inferior frontal regions were thought to play a purely semantic role (Petersen et. al. 1990). However, it has been argued that although damage to the inferior frontal cortex has lead to impaired performance on some tests of semantic processing, it does not tend to impair performance on semantic tasks in the same way that damage to extrasylvian temporal areas seems to, and does not lead to the same severe disturbances of semantic knowledge (Price et. al. 1999). For example, Mummery et. al. (1998) reported that they were unable to find any cases of medial frontal or inferior frontal lesions causing deficits in semantic knowledge. This has lead to the suggestion that inferior frontal regions may form part of a "semantic executive system" that controls the retrieval of semantic information (Price et. al. 1999, page 232; Poldrack et. al. 1999, page 24), or part of a "semantic working memory system" (Poldrack et. al. 1999, page 24; Gabrieli et. al. 1998).

The inferior frontal cortex as part of a semantic executive system

It has been suggested that such a semantic executive system is required to access, maintain and manipulate semantic representations that are represented elsewhere within the cortex (Poldrack et. al. 1999), possibly within the temporal regions that have been associated with semantic knowledge. Poldrack et. al. (1999) describe this system as comprising of three forms of processing, retrieval (involving the arrangement of search cues, and the querying of stored semantic representations according to these search cues), selection (in which competition between retrieved representations is resolved), and

evaluation (whereby the information is synthesised and the appropriate response identified). Inferior frontal regions have been associated with both retrieval and selection processes, although it has been argued that it may be difficult to differentiate these processes as increased retrieval demands are likely to result in increased selection demands (Poldrack et. al. 1999).

Retrieval

It has been reported that left inferior frontal (BA45, 46, and 47) activation is reduced during repeated semantic encoding relative to initial semantic encoding of the same words (Demb et. al. 1995). This reduction only occurred when words were semantically reprocessed, not when they were nonsemantically reprocessed. Based upon these results the authors claim that the left inferior prefrontal cortex forms part of a semantic executive system that contributes to the on-line retrieval of semantic information, as this would account for the apparently enhanced efficiency when accessing information that had recently been processed.

Similar results (Raichle, Fiez, Videen, MacLeod, Pardo, Fox & Petersen, 1994) have been interpreted in a different way. For example, Price (2000) interpreted these results as being linked to the increasing familiarity of a novel task, rather than being directly linked to semantic retrieval. However, this interpretation does not appear to take into account the word-specific nature of the reduced left inferior frontal activation reported by Demb et. al. (1995).

Further support for the idea that left inferior frontal regions may play a role specifically linked to retrieval processes has come from findings that appear to link these regions to working memory processes (Mull & Seyal, 2001), and suggestions that they may form part of a complex network of structures that subserve memory functions (Kapur et. al. 1994). Opinion seems to be divided as to whether the inferior frontal regions play a role in the maintenance of semantic information (and possibly also phonological information) in working memory (Gabrieli et. al. 1998), or in regulating the retrieval of semantic information that may be "stored" in other regions (Saffran & Sholl, 1999, page 262). Besides left inferior frontal regions, right prefrontal cortex (specifically BA10) has also been associated with retrieval processes. MacLeod et. al. (1998) presented a review of the literature surrounding the role of BA10. The majority of the studies considered appear to suggest an involvement of this region in episodic memory retrieval tasks.

Selection

Another review of the literature associated with the role of BA10 concentrated on its possible role in reasoning processes (Christoff, Prabhakaran, Dorfman, Zhao, Kroger, Holyoak & Gabrieli, 2001). Based upon this review it has been claimed that right BA10 appears to be involved with the manipulation of self-generated information, and more specifically with the process of "relational integration" (Christoff et. al. 2001). This refers to the process of considering multiple relations simultaneously, for example in reasoning tasks in which grids of items are presented and missing items have to be inferred by considering relations between items both horizontally and vertically.

This interpretation seems remarkably similar to the role suggested for the inferior frontal cortex in selection during semantic processing. In this case it is assumed that multiple items, such as semantic attributes, are held within working memory and are considered simultaneously (Otten & Rugg, 2001; Davachi, Maril & Wagner, 2001).

An fMRI study addressed the issue of the relative contribution of the inferior frontal regions to retrieval and selection processes (Desmond et. al. 1998). This study used a task in which participants were asked to complete three letter word stems that varied in the number of possible completions. Completion of stems that had few possible completions was thought to rely more strongly upon retrieval processes, whereas completion of stems that had many possible completions was believed to engage selection processes to a greater extent. A double dissociation was observed between the two conditions, whereby frontal regions (including bilateral BA10) were more active during the processing of stems with many possible completions, and right cerebellar regions were more active during the processing of stems with relatively few possible completions. Based upon these findings the authors conclude that the frontal activations reflect selection amongst competing responses, whereas cerebellar activations reflect a sustained search for a response. Based upon these results it is argued that the enhanced inferior frontal response observed for semantic tasks as opposed to non-semantic tasks may result from the necessity to consider more information, and to make the selection of an appropriate response based upon this information (Desmond et. al. 1998; Gabrieli et. al. 1998; Noppeney & Price 2003; Wagner, Paré-Blagoev, Clark & Poldrack, 2001). Similarly enhanced left inferior frontal activation for "difficult" semantic tasks compared to "easy"

semantic tasks may also be explained in terms of more difficult judgements requiring selection amongst more attributes (Roskies et. al. 2001).

There have been other suggestions regarding the role of inferior frontal regions in semantic processing which do not appear to be specifically linked to retrieval, selection, or other working memory processes, but to more abstract reasoning processes such as "hypothesis testing" (Mummery et. al. 1998, p771), the initiation of cognitive strategies (Price et. al. 1999), and willed action (Frith, Friston, Liddle & Frackowiak, 1991a; 1991b). However, the majority of interpretations seem to suggest a role that involves the manipulation of semantic information within working memory.

4.2.6. Functional links between left inferior frontal and temporal regions

In addition to suggesting that the left inferior frontal cortex may play a role in the "online retrieval of semantic information", Demb et. al. (1995) likens this role to that of frontal executive systems in models of working memory. Such executive systems, for example those associated with object and spatial working memory tend to be linked to "storage buffers" in more posterior regions, such as regions within the temporal and parietal lobes (page 5877). It has been suggested that a similar process may occur within the processing of semantic information, whereby frontal executive systems (specifically associated with BA47) may regulate the retrieval of semantic information from temporal and temporo-parietal regions that have been linked to semantic knowledge (Price et. al. 1999).

ERP studies that investigated the time course of semantic processing by comparing semantic tasks to other tasks, such as sentence tasks (Posner & Pavese, 1998), and reading tasks (Abdullaev & Posner, 1998), have reported differential effects within left inferior frontal regions occurring at approximately 200ms after stimulus onset, and differential effects occurring within left temporo-parietal regions occurring much later, at approximately 600ms after stimulus onset. These results have been interpreted within the framework of memory encoding as suggesting that the left inferior frontal cortex supports semantic working memory processes (Otten & Rugg, 2001) and temporo-parietal effects may represent some form of subsequent semantic integration process which would be necessary for obtaining the overall meaning of phrases and sentences (Abdullaev & Posner, 1998; Posner & Pavese, 1998), and forming an "episodic representation" (Otten & Rugg, 2001, page 1150).

It has been argued that this relative timing is also consistent with the interpretation that the left inferior frontal cortex serves to "access, select, gate or retrieve semantic information from semantic stores" within the left temporal cortex (Roskies et. al. 2001, page 839), and that this interpretation is more consistent with lesion findings which seem to suggest a role for the temporal lobes in lexical semantics. Roskies et. al. (2001) speculate that inferior frontal regions may interact with temporal regions by initiating the reactivation of semantic information that is relevant to the task.

4.2.7. Functional links between inferior frontal regions and the cerebellum

A number of authors have reported cerebellar effects that appear to be associated with tasks designed to promote semantic processing. There have been reports of both bilateral (McDermott et. al. 2003) and right lateralised (Vandenberghe et. al. 1996; Roskies et. al. 2001) cerebellar effects. As with inferior frontal effects, cerebellar effects appear to be associated with semantic effects in general, rather than semantic effects specific to reading (Vandenberghe et. al. 1996), and do not seem to be specific to the processing of visually presented stimuli (Noppeney & Price, 2003).

Despite these findings, there have been exceptions whereby phonological tasks have been associated with bilateral (Paulesu et. al. 1993) and left lateralised cerebellar effects (Mummery et. al. 1998). Although implicit semantic processing may account for such reports, it has also been suggested that these findings may be attributed to the automatic involvement of regions thought to be linked to motor aspects of speech planning and execution (Paulesu et. al. 1993). However it is unclear why the syllable counting task employed by Mummery et. al. (1998) should produce these effects, as these have not been reported when the task has been used elsewhere (Otten & Rugg, 2001), although it is possible that differences between the control tasks may account for this discrepancy.

Although cerebellar effects have been linked to motor processes such as response generation, there is increasing evidence to suggest that cerebellar regions, specifically within the right cerebellum, may play an important role in cognitive processes that is independent of motor aspects of response preparation. For example, Desmond et. al. (1998) reported a dissociation between left frontal and right cerebellar effects during a stem completion task, whereby left frontal activation increased for stems with many possible completions, and right cerebellar activation increased for the processing of stems with

relatively few possible completions. If cerebellar effects were purely associated with motor aspects of response preparation then cerebellar activation would be expected to increase for stems with many possible completions, and therefore many possible responses. Based upon these findings the authors suggest that the cerebellar effects reflect a greater level of subvocal articulatory rehearsal that corresponds to a sustained demand on working memory that is associated with the task of searching for stem completions.

Similarly Roskies et. al. (2001) reported that both left inferior (BA47) activation and right cerebellar activation was greater within a "hard" semantic condition than an "easy" semantic condition. Both of these conditions involved category judgements, with the "hard" condition involving category members that were less typical. It is not immediately obvious how phonological processes could have accounted for the cerebellar differences, unless stimuli from the "hard" semantic condition were held in working memory for longer, leading to more sustained subvocal rehearsal, which would be consistent with the interpretation offered by Desmond et. al. 1998 in response to the findings of their stem completion study.

However, this interpretation would imply that the cerebellar effects arise from phonological processes, which is hard to resolve with findings of right cerebellar effects linked specifically to semantic tasks when compared to phonological tasks such as making rhyming decisions (Roskies et. al. 2001). Although the precise role of the cerebellum within semantic processing is unclear, it does seem that for semantic tasks, the right cerebellum is functionally related to the left prefrontal cortex. Not only have both these regions been identified as contributing to semantic networks (Vandenberghe et. al. 1996), activations within both of these regions have been found to decrease while participants repeatedly generate verbs in response to nouns (Raichle et. al. 1994) suggesting a functional correlation between these two regions during semantic processing (Desmond et. al. 1998).

4.2.8, Other semantic regions, anterior cingulate, thalamus, and motor regions

Task dependent differential effects have also been reported to occur within the anterior cingulate. These effects have been associated with semantic task conditions both when compared to low-level nonsemantic tasks (Poldrack et. al. 1999), and when compared to phonological tasks (Petersen et. al. 1989; Roskies et. al. 2001). They do not appear to be modality specific (Petersen et. al. 1989). However, enhanced anterior

cingulate activation has also been reported for phonological tasks when compared to low-level, orthographic tasks (Poldrack et. al. 1999). Rather than being specifically linked to semantic processing, these effects have been observed for a range of tasks, the level of anterior cingulate activation has been associated with task difficulty, and it seems to be generally accepted that these effects are more likely to be the result of attentional demands (Bush, Luu & Posner, 2000). It seems likely that these effects correspond to the frontal midline theta rhythm, which has also been observed using EEG during tasks requiring focussed attention. MEG evidence suggests that this activity originates from a region between the superior frontal gyrus and the anterior cingulate (Ishii, Shinosaki, Ukai, Inouye, Ishihara, Yoshimine, Hirabuki, Asada, Kihara, Robinson & Takeda, 1999; Asada, Fukuda, Tsunoda, Yamaguchi & Tonoike, 1999).

Although it has been suggested that anterior cingulate effects may occur even in anticipation of cognitively demanding tasks (Bush et. al. 2000), when comparing a use generation task with a reading task, Abdullaev & Posner (1998) observed a significant difference between ERPs from the two conditions at approximately 170ms post stimulus onset ($p<0.001$). Using analysis of topographic maps and dipole sources together with PET data, these effects were localised to the anterior cingulate. These differential effects were reported to precede those observed within the left inferior frontal cortex by approximately 50ms and strong reciprocal interconnections have been identified between the anterior cingulate and lateral prefrontal cortex (Devinsky, Morrell & Vogt, 1995).

4.3, Phonological networks

4.3.1, Phonological processing and parietal / temporal regions

Studies designed to identify the neural correlates of phonological processing have tended to highlight the importance of parietal regions (specifically the supramarginal gyrus and BA39/40) in tasks thought to require processing of the sound structure of words and letters (Paulesu et. al. 1993). Bilateral activation within the supramarginal gyrus (BA40) and posterior parietal regions has been observed for syllable counting tasks when compared to various semantic tasks (Mummery et. al. 1998; Otten & Rugg, 2001). Otten, Henson & Rugg (2001) reported bilateral effects within BA40 in response to an alphabetic task in which participants were required to determine whether the first and last letters of a word are in alphabetical order. Bilateral effects within BA40 have even been observed when participants were required to "attend to the relations" between rhyming words, compared to words which were semantically linked (McDermott et. al. 2003).

There have also been reports of lesions within the left supramarginal gyrus producing phonological agraphia, whereby patients can write words from dictation, but not nonwords (Shallice & Burgess, 1991) suggesting it is an impairment linked to phonological processing. Similarly, lesions observed within individuals with phonological dyslexia have been found to extend into the supramarginal gyrus (Marin, 1980).

On the basis of the results of the study by Paulesu et. al. (1993) previously discussed, in which the authors investigated component processes within the "articulatory loop", it was claimed that whereas Broca's area is associated with a subvocal rehearsal system, the left supramarginal gyrus may represent the primary location of a "phonological store". This interpretation is consistent with their finding that these regions showed greater activation during a phonological short-term memory task than during a rhyming task thought to rely upon subvocal rehearsal systems but not the "phonological store".

4.3.2, Posterior superior temporal regions (Wernicke's area)

Based upon a review of the literature, Price (2000) acknowledged that phonologically related parietal effects extend to left posterior superior temporal cortical regions (which encompass Wernicke's area). Similarly, Petersen et. al. (1989) reported temporo-parietal effects, near to the cortical area associated with auditory word input, which seemed to be linked to phonological processing.

Démonet, Fiez, Paulesu, Petersen & Zatorre (1996) have described an "activated triad" of regions that have tended to be associated with phonological processing tasks. This consists of Broca's area, the left supramarginal gyrus, and Wernicke's area. These three regions have been identified by both visual and auditory studies that have investigated phonological processing (Démonet et. al. 1992; Paulesu et. al. 1993). Activation has been reported within Wernicke's area in the left superior temporal gyrus for a number of phonological tasks, including pronunciation tasks (Rumsey, Horwitz, Donohue, Nace, Maisog & Andreason, 1997), and rhyming tasks (Paulesu et. al. 1993; Temple et. al. 2001).

Originally lesions in Wernicke's area within the left posterior-superior-temporal cortex were associated with impaired speech comprehension, with less impairment in the production of well articulated speech. Wernicke's area was therefore associated primarily with speech comprehension. It has subsequently been acknowledged that patients with

Wernicke's aphasia also show impaired articulation of speech sounds (Price et. al. 1999), and that comprehension deficits involving both auditory and visual material are typically associated with large left temporo-parietal lesions that extend beyond Wernicke's area. This would imply that rather than being specifically linked to comprehension, Wernicke's area may play a role associated with the "auditory images of speech" (Price, 2000), and more closely allied to phonological processing.

These effects appear to be distinct from the temporal effects observed for semantic tasks. It has been observed that the atrophic changes observed in the temporal lobes of patients with "semantic dementia" (associated with impaired word comprehension and impaired performance on semantic tasks) do not extend to the superior temporal areas, and phonological abilities are preserved (Hodges et. al. 1992). A dissociation has been observed between these two regions as a result of studies of lesions associated with surface and phonological dyslexia. Whereas surface dyslexia has been associated with left inferior temporal lesions (Vanier & Caplan, 1985), phonological dyslexia has been linked to more superior lesions (Marin, 1980). These dissociations have lead to the conclusion that the left inferior temporal cortex may be involved in a "semantic route to reading", and the left superior temporal cortex involved in a "nonsemantic route to reading" (Price, 2000, page 348).

Neuroimaging studies have also revealed a dissociation between Wernicke's area and the left posterior inferior temporal cortex associated with semantic processing. Following a review of various neuroimaging studies, Price (2000) concluded that while Wernicke's area is consistently activated by heard word repetition tasks, it is not consistently activated by reading. However, the left posterior inferior temporal cortex does appear to be consistently activated by reading but not heard word repetition. This is also supported by the observation that Wernicke's area is more active for reading than picture naming, whereas the left posterior inferior temporal lobe is activated both by reading and picture naming (Bookheimer et. al. 1995; Price, 2000). Whereas picture naming requires semantic analysis, reading does not necessarily require semantic analysis (for example, as in pseudoword reading). This provides further support for the theory that the left posterior inferior temporal area is more consistent with a semantic route and Wernicke's area consistent with a non-semantic route.

It has been suggested that the "nonsemantic route" may involve phonological processing (Price, 2000). Wernicke's area has been found to be more active when Italian

speakers read Italian than when English speakers read English, which may be a consequence of the greater consistency between orthography and phonology in Italian than in English, which may lead to a greater involvement of Wernicke's area (Paulesu et. al. 2000). Similarly, in cases of receptive aphasia, patients with damage to left superior posterior temporal regions have been found to show impairments in processing speech sounds (Basso, Casati & Vignolo, 1977), possibly related to the fact that primary auditory areas are located within the temporal lobes, and so there will be direct connections to auditory association areas (Burton, 2001).

4.3.3, The time course of differential effects

In view of findings, such as those reported by Paulesu et. al. (1993) which suggest that superior temporal/parietal regions may be associated with a "phonological store" and Broca's area involved with subvocal rehearsal mechanisms, it seems reasonable to assume that phonological superior temporal/parietal effects should precede those occurring within Broca's area (Burton, 2001). It seems that there is a need for studies specifically addressing the time course of such phonological processing effects in order to investigate these claims.

4.3.4, Insula

It is also possible that the insula may play a role in phonological processing. It has been reported that regions within the left anterior and middle insula were preferentially active during a rhyme task as opposed to a synonym task, and suggested that this region may be involved in "inner hearing" of phonological information, or covert articulatory rehearsal (Paulesu et. al. 1993; Roskies et. al. 2001). However, the results of lesion studies indicate that this region may play a role more closely linked to the motor planning of speech. Dronkers (1996), for example, considered lesion data from 44 patients, 25 of whom had apraxia of speech that involved articulatory deficits in the absence of any difficulty in perceiving or recognising speech sounds. All of the patients with articulatory planning deficits were found to have lesions that included a discrete region of the left precentral gyrus of the insula. This region was completely spared in each of the patients who failed to show such deficits. This double dissociation was interpreted as showing a specialisation of the insula for motor planning of speech.

4.3.5, Regions associated with motor control

Similarly, Paulesu et. al. (1993) reported activation within areas thought to be devoted to motor aspects of speech planning and execution, for example, the supplementary motor area (SMA), cerebellum and primary sensorimotor areas of mouth and larynx (BA4, 3, 2, 1 and BA6), for phonological tasks, even in the absence of overt speech. Other authors have reported an involvement of regions within the motor cortex in phonological tasks, which has been attributed to movement associated with subvocal articulation or automatic speech preparation (Roskies et. al. 2001).

Similarly, regions within BA44/6 that have been found to be active during tasks involving the repetition of words, compared to listening to words, have also been shown to be involved in preparing finger movements and imagining movements. It has therefore been argued that that these regions may be important for preparing intricate motor plans including those required for speech (Price et. al. 1999).

4.4, Summary

The results of various semantic/phonological task manipulation studies are presented within Appendices 4.1-4.14. Due to the imaging techniques available, investigation into semantic and phonological processing has tended to focus upon the analysis of differential effects within the spatial domain, with relatively few studies addressing frequency information associated with these effects, or their time course. The relative timing of frontal, temporal/parietal and cerebellar effects is of particular interest as this may impact upon models of semantic and phonological processing within the brain.

Chapter 5

Study 1: Task-specific semantic and phonological processing of visually presented words, Synthetic Aperture Magnetometry (SAM) techniques applied to Magnetoencephalography data.

5.1, Abstract

Due to the imaging techniques available, investigation into semantic and phonological processing has tended to focus on the analysis of differential effects within the spatial domain. Such fMRI, PET and lesion studies have identified a number of regions as showing differential effects associated with either semantic or phonological processing. Whereas left inferior and middle temporal regions (specifically BA20) have been frequently associated with "semantic stores", left parietal regions (specifically BA40) have been described as representing "phonological stores". Cerebellar regions have been associated with the process of sub-vocal rehearsal, but there are also reports of cerebellar effects being specifically linked to apparently semantic tasks. Frontal effects have been associated with both semantic and phonological processing. Although the specificity of these regions seems to be a matter of debate, there have been a number of claims that certain inferior/prefrontal regions (specifically BA10 and BA47) may form part of a "semantic executive system". This has lead to speculation regarding the possible role of such a system in the maintenance of semantic information within working memory, the regulation of retrieval and selection processes, and its possible interaction with "information stores".

The same stimulus set of visually presented nouns were displayed within both a semantic task condition, (in which participants were required to make a living/nonliving decision), and a phonological task condition (in which participants counted the number of syllables within each word). Participants were instructed as to which task to perform by single word task primes that appeared prior to each stimulus being displayed. A behavioural study was conducted which took the form of a recognition memory study. This produced results that are in keeping with a "level of processing" effect, whereby recognition memory performance tends to be better for semantically encoded words than for phonologically encoded words. These results validated the paradigm for use within an MEG study designed to investigate the neural correlates of these two forms of processing.

Within both task conditions statistically significant ($p<0.05$) left frontal (BA10) ERD was observed, at the group level, within the gamma frequency range (30-50Hz). This

occurred earlier within the semantic task condition (350-550ms) than within the phonological task condition (500-700ms). The phonological condition was also associated with statistically significant left inferior frontal ERD within BA45 (14-20Hz, 500-700ms).

Both task conditions were associated with statistically significant ($p<0.05$) ERD within the left inferior parietal region BA40, although this tended to occur earlier within the phonological condition (350-550ms) than the semantic condition. This is consistent with the suggestion that this region may be associated with "phonological stores", as the ERD observed within the semantic task may represent delayed implicit phonological processing occurring irrespective of task demands.

Task-dependent differential effects were also observed within the right cerebellum. In keeping with the suggestion that the cerebellum may play a role associated with sub-vocal rehearsal, right cerebellar ERD was specific to the phonological task. This was observed within the 14-20Hz frequency band, and both the 350-550ms and 500-700ms time windows, which is also consistent with the notion of a sustained process of sub-vocal rehearsal.

The spatial-temporal dynamics of the frontal and temporal/parietal differential effects within the two conditions have implications for theories regarding the interaction between frontal "executive" systems and semantic/phonological "stores". Within the phonological task condition, ERD within the left inferior parietal region associated with "phonological stores" (BA40) preceded left frontal ERD. However, within the semantic condition, frontal ERD preceded ERD observed within temporal "semantic stores", suggesting that there is a dissociation between the use of such "stores" within semantic and phonological processing.

5.2, Behavioural Study: Introduction

One behavioural measure that can be used to differentiate between semantic and phonological processing tasks is recognition memory for items that have been encoded during an incidental learning phase in which these tasks are used. This is based on the "levels of processing" framework (Craik & Lockhart, 1972), in which there is a hierarchy of processing stages. Phonological processing has been described as a shallow form of processing (Perrin & García-Larrea, 2003; Fujii, Okuda, Tsukiura, Ohtake, Suzuki, Kawashima, Itoh, Fukuda & Yamadori, 2002), whereas semantic processing is treated as a deeper level of processing, and described as involving "enrichment or elaboration" (Craik & Lockhart, 1972). Craik and Lockhart reported that the retention of a word is determined by the level at which it is processed, with deeper levels of processing associated with longer lasting memory traces. Subsequently this has become a standard framework, for example for use within memory research (for example, Kapur et. al. 1994).

Chapter 5 describes an investigation into the neural correlates of semantic and phonological processing. In order to ensure that the paradigm and stimuli used within this study were capable of promoting different types of processing, it was first necessary to demonstrate a behavioural difference between the two task conditions. A "levels of processing" approach was used to demonstrate this dissociation.

Participants performed semantic and phonological tasks using single word target stimuli. Task primes presented prior to the onset of each target stimulus informed participants which task to perform on the following stimulus. This formed an incidental learning phase, which was immediately followed by a recognition memory phase. It was anticipated that, in line with the "levels of processing" effect, more of the semantically encoded words would be successfully recognised than the phonologically encoded words.

5.3, Behavioural Study: Method

5.3.1, Participants

Fifty undergraduate students participated in this study (46 females, 4 males). Participants were either in their first or second year of a psychology degree at Aston University, and all claimed English to be their first language. 44 of the participants were right-handed and 6 were left-handed.

5.3.2, Stimuli

The stimulus set consisted of 128 nouns (see Appendix 5.1). 64 words were names of animals, birds or fish, and the other 64 were names of nonliving entities. 32 of the "living" words had one syllable, and 32 had two syllables, and the same was true for the "nonliving" words. Words from each of these four categories were matched in terms of number of letters, and word frequency score according to Kucera & Francis (1967) written word frequency norms given in the MRC Psycholinguistic database (1987).

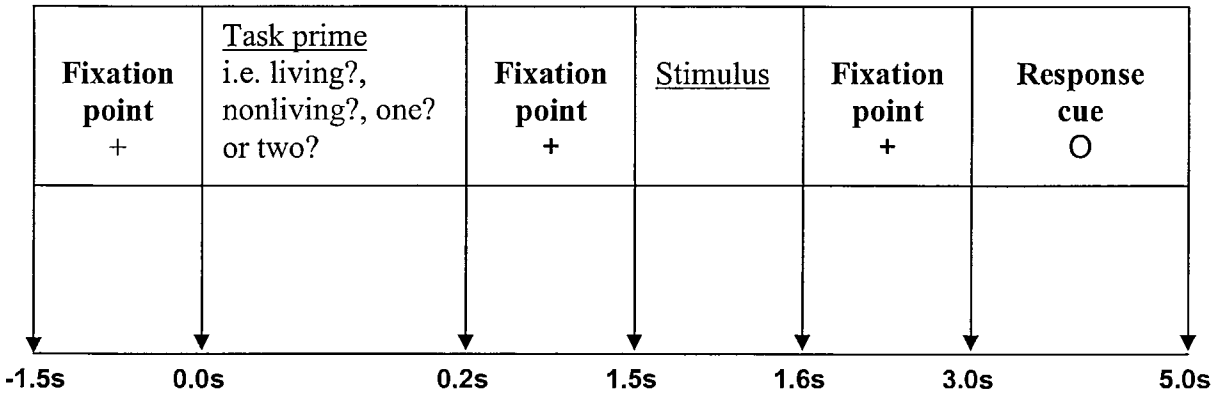
The recognition phase involved another set of 128 nouns (see Appendix 5.2), which were matched to the first set in terms of the number of syllables, whether they were "living" or "nonliving", word frequency, and number of letters.

5.3.3, Procedure

Participants initially undertook an incidental learning phase, during which the stimuli were presented on a computer monitor for 100ms, in random order. Participants were required to make a semantic decision about half of the words and a phonological decision about the other half. The words used in each task condition were counterbalanced across participants. The semantic task involved indicating whether the word referred to living or nonliving entity, and the phonological task required participants to count the number of syllables. Tasks were primed by single-word questions that were presented for 200ms prior to stimulus presentation. These were "living?", "nonliving?" "one?" and "two?". All words were presented in black, with a white background, and the stimuli were displayed inside single line frame in order to differentiate them from the task primes. The questions were counterbalanced across stimulus conditions so that, for example, there were an equal number of two syllable "living" words appearing with each of the task priming questions. Cued yes/no responses were made via a button press. The response cue was used for consistency with the MEG study (although within the MEG study responses were made by a finger movement as opposed to a button press).

Figure 5.1 shows the stimulus sequence. Participants were asked to fixate on a cross in the centre of the screen for 1.5s. The task prime was then displayed for 0.2s, followed by the fixation cross for 1.3s. The target stimulus was then presented for 0.1s, the fixation cross was shown for 1.4s before the response cue (a small circle in the centre of the screen) was displayed for 2.0s.

Figure 5.1, The stimulus sequence



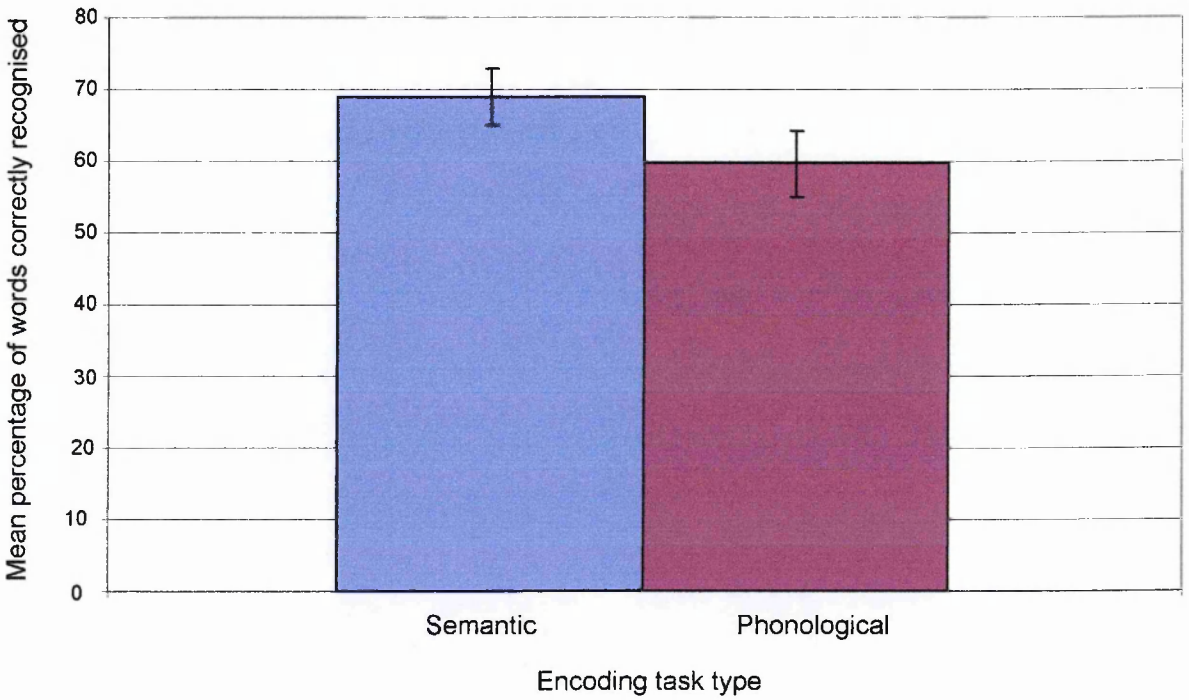
Participants completed a practice run of 7 sequences prior to starting the encoding phase. When participants made an incorrect response during the practice run they were immediately informed of the correct response, with a brief explanation. Participants were given the opportunity to ask questions about the procedure before they began the encoding phase.

Following the encoding (incidental learning) phase, participants were informed about the recognition phase. The previously seen stimuli were shown in random order together with the new stimuli. Participants were asked to indicate, via a button press, whether or not the word had appeared in the previous phase. Each word was displayed until the participant made a response. In this way two recognition scores were obtained for each subject: the number of correctly recognised words that had first appeared within the semantic task condition, and the number of correctly recognised words that had originally appeared in the phonological task condition.

5.4. Behavioural Study: Results

The mean percentage of semantically encoded words that were correctly recognised was 68.88% (SD=13.84, N=50), whereas the mean percentage of phonologically encoded words that were correctly recognised was 59.66% (SD=16.23, N=50). Figure 5.2 shows the mean percentage of words recognised in each of the two encoding conditions. The error bars indicate the 95% confidence interval for the true population mean for each condition (calculated from the Standard Errors).

Figure 5.2. The mean percentage of words correctly recognised for each of the two encoding task conditions. The error bars represent the 95% confidence interval for the true population mean, calculated from the Standard Errors.



A one-way within subjects ANOVA was conducted on the recognition scores, and revealed a significant main effect of task type (i.e. semantic or phonological) ($F_{(1,98)} = 9.342$, $p<0.01$) with participants recognising more of the semantically encoding words than the phonologically encoded words.

5.5, Behavioural Study: Conclusion

In line with the level of processing memory effect identified by Craik & Lockhart (1972), during the recognition phase participants recognised significantly ($p<0.01$) more of the semantically encoded words than the phonologically encoded words.

It seems unlikely that confounding variables could have been responsible for this effect. Words were matched for word length and frequency (according to the Kucera & Francis, 1967 written word frequency norms given in the MRC Psycholinguistic database, 1987). Although these frequency scores were not obtained recently, there is evidence that there is a high level of consistency between these scores and those obtained in 1995 for the CELEX English linguistic database, and those obtained in 2002 using internet search engines (Blair & Urland, 2002). The task requirements (i.e. the specific question asked and the response required) were counterbalanced across the two task conditions in an attempt to reduce the effects of any confounds. An attempt was also made to control for any confounds associated with the choice of stimuli by counterbalancing the words appearing within each of the two task conditions across participants.

Therefore, having demonstrated a depth of processing memory effect, it was concluded that this paradigm and stimulus set was appropriate for use within a neuroimaging study designed to compare different levels of processing.

5.6, MEG Study: Method

5.6.1, Participants

Ten right handed participants gave informed consent to participate in this study (6 females, 4 males). Participants were either postgraduate students or university lecturers, with English as their native language. All participants had normal, or corrected-to-normal vision, and none had taken part in the behavioural study. Each participant had previously had an anatomical MR volume scan.

5.6.2, Stimuli

Task primes: As in the behavioural study, there were four task primes, "living?" and "nonliving?" which were used to prime the semantic task, and "one?" and "two?" which were used to prime the phonological task

Single word targets: The stimulus set consisted of 96 nouns taken from those used within the behavioural study. 48 of the words were names of animals, birds or fish, and the other 48 were names of non-living entities. 24 of the "living" words had one syllable, and 24 had two syllables. The same was true of the "nonliving" nouns. Words from each of these four categories were matched according to number of letters and word frequency score taken from Kucera & Francis (1967) written word frequency norms given in the MRC Psycholinguistic Database (1987).

5.6.3, Procedure

The procedure was identical to that employed in the behavioural study, with the two task conditions being primed in a trial-by-trial manner (Figure 5.1). However, as the recognition phase was not required for the MEG study, each word was presented twice: once in each of the two task conditions. Before entering the shielded room, participants completed the 7-sequence practice run used for the behavioural study.

Cued yes/no responses were made via movement of the left index finger. The response was required in order to ensure that participants were carrying out the appropriate task, and the cue was included in an attempt to keep motor activity temporally separate from word processing. The left hand was placed on the armrest with the index finger strapped to a Perspex frame so that a finger movement interrupted a laser beam, and the

number of movements could be recorded. Participants were asked move their finger twice to make a "yes" response, and once to make a "no" response.

5.6.4. MEG recording and coregistration with MRI data

MEG data was collected using a 151-channel CTF Omega system (CTF Systems Inc., Port Coquitlam, Canada). The data was collected at a sampling rate of 625Hz. Following data acquisition the shape of the participants head was digitised using a 3-D digitiser (Polhemus Isotrack). This surface was matched to that extracted from the participant's anatomical MRI, using Align (www.ece.drexel.edu/ICVC/Align/align11.html) so that the MEG data obtained from each participant was coregistered with their anatomical MRI scan.

5.6.5. Data Analysis

Epochs containing eye blink artefacts were identified by visual inspection, and omitted from further analysis. Within this study the epoch of interest was that associated with the presentation of the target stimulus. Three time windows of interest were identified from the literature (50-250ms, 350-550ms and 500-700ms post-stimulus onset). These time windows were therefore used within SAM analysis, in order to draw comparisons both between the two conditions, and also between each condition and 200ms of prestimulus time (which in this case occurred prior to the presentation of the task prime). For each of these comparisons, and for each participant, a 3D statistical parametric map was produced for each of the frequency bands (8-13Hz, 14-20Hz, 20-30Hz, 30-40Hz and 40-50Hz). These images were averaged using Group SAM and the statistical significance of differential effects assessed using SnPM (the techniques are described within Chapter 2).

5.7, MEG Study: Results

5.7.1, Behavioural results.

All participants completed the practice run with 100% accuracy. For the main study the mean percentage accuracy was 98.0% (SD = 1.2%) for the semantic task, and 97.6% (SD = 2.4%) for the phonological task.

MEG Results

The co-ordinates of each of the voxels showing significant effects ($p<0.05$) for the two task conditions relative to the prestimulus baseline, identified using Statistical NonParametric Mapping, are presented in the Tables 5.1-5.3. Voxels lying within sensorimotor regions such as BA2 and BA6 were excluded from further analysis. In this way voxels were identified for both the semantic and the phonological task conditions. The results of the semantic v phonologocial comparisons failed to reach statistical significance ($p<0.05$). For voxels in which significant effects were observed in either the semantic or phonolgical task conditions compared to the prestimulus baseline, t vaules associated with the semantic v phonological comparisons are presented within tables 5.1-5.3.

Table 5.1, The co-ordinates of the voxels showing significant effects ($p<0.05$) for the two task conditions relative to the prestimulus baseline, identified using Statistical NonParametric Mapping, for the 50-250ms time window. None of the differential effects observed within the semantic v phonological comparison reached statistical significance ($p<0.05$). Itallics indicate the results of the semantic v phonological comparison for voxels in which significant effects were observed within either of the task conditions with respect to the prestimulus baseline.

50-250ms	**Semantic versus Baseline**	**Phonological versus Baseline**	**Semantic v Phonological**
8-13Hz	-	-	-
14-20Hz	-	-	-
20-30Hz	-	-	-
30-40Hz	-	Left superior parietal lobule BA7 -27, -72, 66	*Left superior parietal lobule BA7 (-27, -72, 66): t=0.46*
	-	Left paracentral lobule BA6 -3, -33, 75	*Left paracentral lobule BA6 (-3, -33, 75): t=0.42*
40-50Hz	-	-	-

Table 5.2, The co-ordinates of the voxels showing significant effects ($p<0.05$) for the two task conditions relative to the prestimulus baseline, identified using Statistical NonParametric Mapping, for the 350-550ms time window.

350-550ms	Semantic versus Baseline	Phonological versus Baseline	Semantic v Phonological
8-13Hz	-	Left frontal precentral gyrus next to BA6 -72, -9, 30	*Left frontal precentral gyrus (-72, -9, 30): t=0.53*
14-20Hz	Right superior temporal gyrus 51, -12, -3	Right cerebellum 30, -87, -48	*Right superior temporal gyrus (51, -12, -3): t=0.49* *Right cerebellum (30, -87, -48): t=-0.27*
		Left occipital lobe next to BA37 middle temporal gyrus -60, -72, 3	*Left occipital lobe/middle temporal gyrus (-60, -72, 3): t=-0.90*
20-30Hz	Left middle temporal gyrus BA39 -36, -75, 15, -54, -78, 24	Left inferior parietal lobule BA40 -36, -48, 39, -45, -60, 54	*Left middle temporal gyrus BA39* *(-36, -75, 15): t=-1.69* *(-54, -78, 24): t=-1.61* *Left inferior parietal lobule BA40* *(-36, -48, 39): t=-0.09* *(-45, -60, 54): t=-1.70*
	Left parietal precuneus -3, -63, 33, -12, -87, 54		*Left parietal precuneus* *(-3, -63, 33): t=-0.85* *(-12, -87, 54): t=-0.94*

30-40Hz	-	Left middle frontal gyrus near BA6 -27, 0, 63	*Left middle frontal gyrus near BA6* *(-27, 0, 63): t=-1.93*
		Right precentral gyrus frontal BA44 57, 9, 9	*Right precentral gyrus frontal BA44* *(57, 9, 9): t=-0.62*
40-50Hz	Left superior frontal gyrus BA10 -15, 69, 33	-	*Left superior frontal gyrus BA10 (-15, 69, 33):* *t=-0.03*

Table 5.3, The co-ordinates of the voxels showing significant effects ($p<0.05$) for the two task conditions relative to the prestimulus baseline, identified using Statistical NonParametric Mapping, for the 500-700ms time window.

500-700ms	**Semantic versus Baseline**	**Phonological versus Baseline**	**Semantic v Phonological**
8-13Hz	-	-	-
14-20Hz	-	Left inferior frontal gyrus near BA45 -57, 24, 12	*Left inferior frontal gyrus near BA45* *(-57, 24, 12): t=0.75*
		Right fusiform gyrus BA37 51, -48, -21	*Right fusiform gyrus BA37* *(51, -48, -21): t=0.37*
		Right cerebellum 48, -54, -38	*Right cerebellum* *(48, -54, -38): t=0.42*

20-30Hz	Left inferior parietal lobule BA40 -51, -66, 48	-	*Left inferior parietal lobule BA40* *(-51, -66, 48): t=-1.53*
30-40Hz	-	Right parietal postcentral gyrus near BA2 60, -30, 51	*Right parietal postcentral gyrus near* *BA2 (60, -30, 51) t=-1.46*
		Left middle frontal gyrus near BA10 -39, 39, 30	*Left middle frontal gyrus near BA10* *(-39, 39, 30) t=-0.44*
40-50Hz	-	-	-

5.7.2, Left Temporal effects

SnPM results revealed that both the semantic (figure 5.3) and phonological (figure 5.4) tasks were associated with statistically significant group event-related desynchronisation within the left middle temporal gyrus, in the region of BA37 / BA39. Both of these effects occurred between 350ms and 550ms post stimulus onset, and within the beta frequency band (20-30Hz in the case of the semantic task condition, and 14-20Hz for the phonological task).

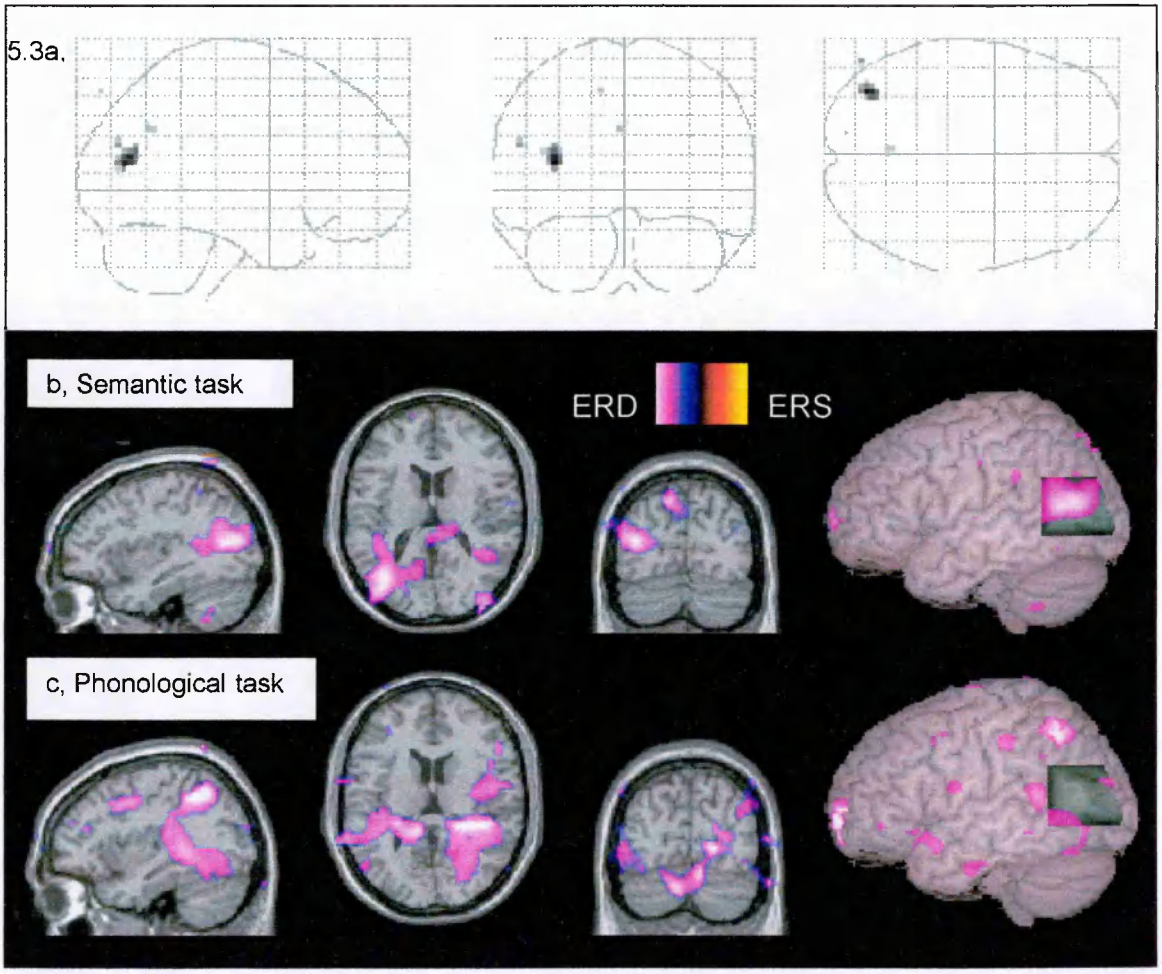


Figure 5.3. a) Glass brain images showing the location of the two left middle temporal voxels identified within the 20-30Hz, 350-550ms semantic versus prestimulus comparison as showing statistically significant differential effects ($p<0.05$, talairach co-ordinates –36, -75, 15, and –54, -78, 24).

b) Group SAM rfx images for the 20-30Hz, 350-550ms semantic versus prestimulus comparison (where the left middle temporal voxel showing the most significant differential effect was associated with a t value of –4.92), and

c) Group SAM rfx images for the phonological versus prestimulus comparison (where the same voxel was associated with a t value of –1.61). Both Group SAM rfx images show values corresponding to $-3>t>3$.

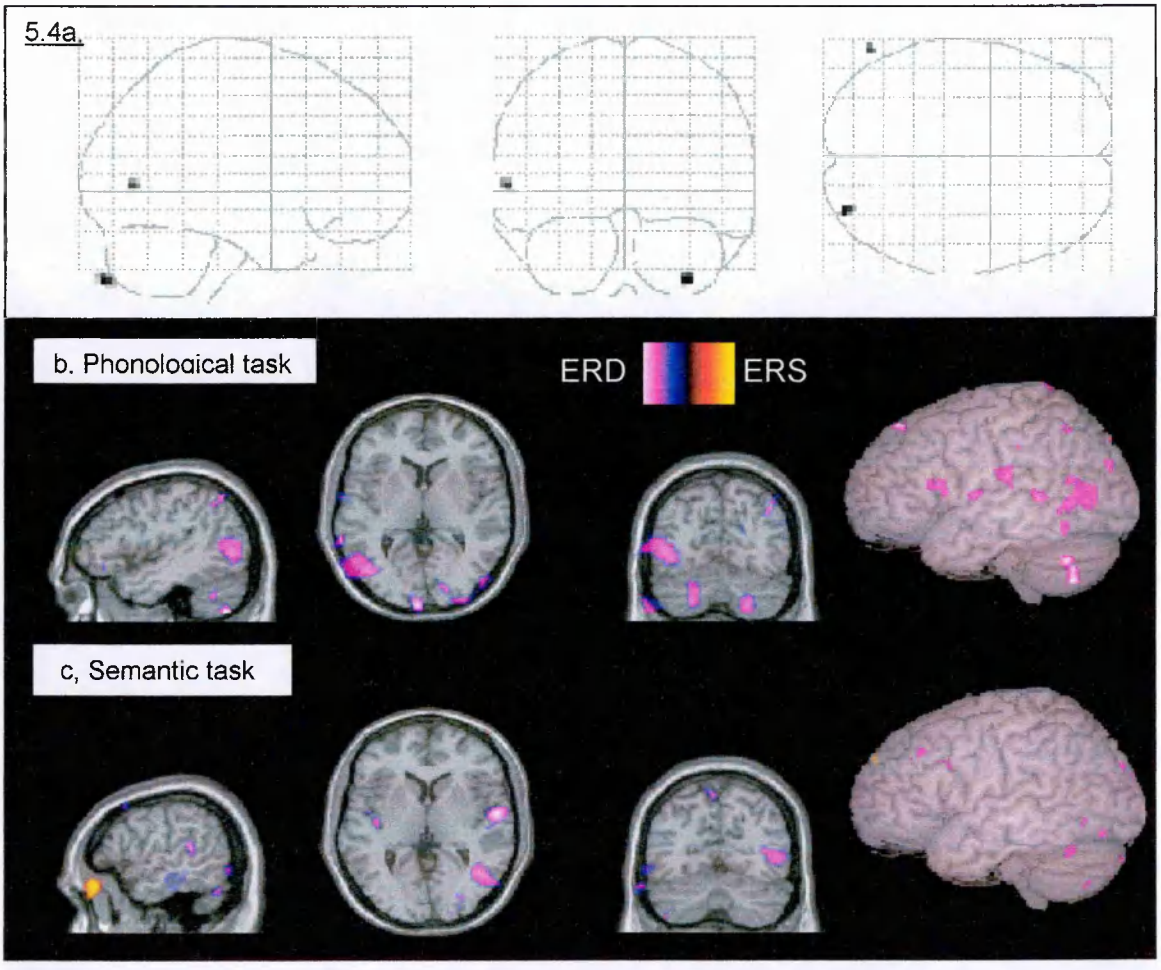


Figure 5.4. a) Glass brain images showing the location of the left temporal voxel identified within the 14-20Hz, 350-550ms, phonological versus prestimulus comparison. This voxel is slightly more inferior to that identified within the semantic task condition (figure 5.3), (talairach co-ordinates –60, -72, 3) and bordered the occipital lobe.
b) Group SAM rfx images for the 14-20Hz, 350-550ms phonological versus prestimulus comparison (where the left occipito-temporal voxel identified using SnPM was associated with a t value of –3.06, and
c) the semantic versus prestimulus comparison (where the same voxel was associated with a t value of –1.66). The images show values corresponding to $-3>t>3$.

For illustration, Mann Whitney time-frequency representations were produced for virtual electrodes placed at the location of each of these peaks. An example representation for a virtual electrode placed at a temporal peak in one participant is displayed in figure 5.5a. This shows that for this participant, the power decrease within the 17-19Hz frequency band was associated with a Mann Whitney statistic of $Z>2$ (i.e. $p<0.05$), between 430ms and 600ms in the semantic condition.

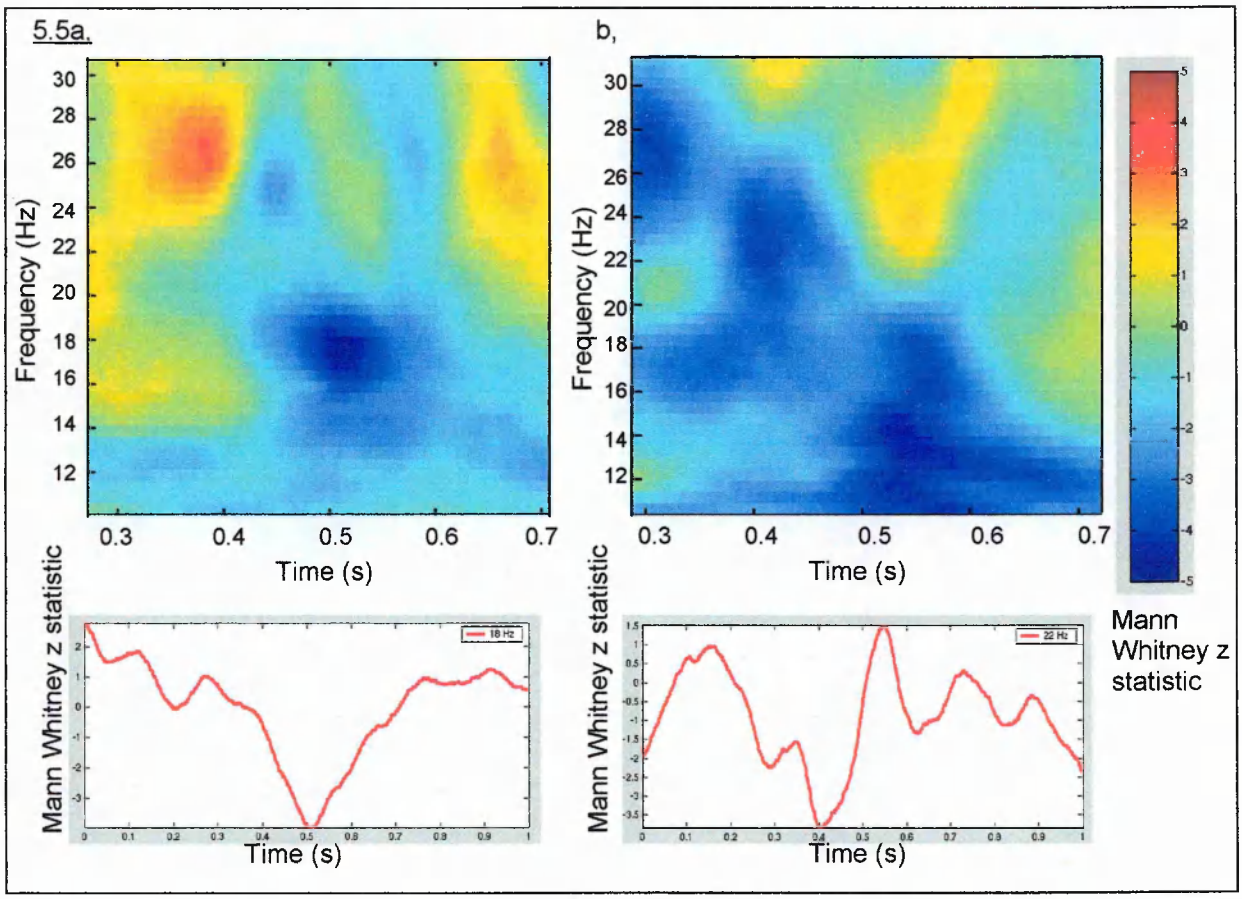


Figure 5.5. a) An example time-frequency Mann Whitney spectrogram for the semantic versus prestimulus comparison for a virtual electrode placed within the left temporal region for one participant. A power decrease in the 14-20Hz frequency band is observed at approximately 500ms. The colour represents the Mann Whitney z statistic. The line graph shows the Mann Whitney z statistic as a function of time for the 17Hz to 19Hz frequency band for the semantic versus prestimulus comparison for the same virtual electrode.

b) An example time-frequency Mann Whitney spectrogram for the phonological task versus prestimulus comparison for a virtual electrode placed within the left temporal region for one participant. A power decrease is observed within the beta frequency band (at around 14Hz), at approximately 550ms after stimulus onset. The line graph shows the Mann Whitney z statistic as a function of time for the 21Hz to 23Hz frequency band for the phonological versus prestimulus comparison for a virtual electrode placed within the left temporal region of one participant.

Again Mann Whitney time-frequency representations were produced for virtual electrodes placed at the location of the phonological peaks. An example is displayed in figure 5.5b. This shows that for the 21-23Hz frequency band the Mann Whitney $Z > 2$ (i.e. $p<0.05$) between 360ms and 480ms.

5.7.3, Right Temporal effects

SnPM analysis also revealed that the semantic task was associated with statistically significant ($p<0.05$) group event-related desynchronisation within the right superior temporal gyrus, (figures 5.6). This effect occurred within the 350-550ms, 14-20Hz comparison.

5.7.4, Parietal effects

Again both the phonological (figure 5.7) and the semantic (figure 5.8) task conditions were associated with statistically significant event-related desynchronisation within the left inferior parietal lobule, BA40 ($p<0.05$). The phonological parietal effect occurred earlier than the semantic effect (within the 350 to 550ms time window for the phonological versus prestimulus comparison, and in the 500 to 700ms time window for the semantic versus prestimulus comparison). Both of these effects occurred within the 20-30Hz beta frequency band.

Examples of Mann Whitney time-frequency representations produced for virtual electrodes placed at the location of each of these peaks are displayed in figure 5.9. This shows that for the 24-26Hz frequency band $Z > 2$ (i.e. $p<0.05$) between 420ms and 500ms in the case of the phonological versus prestimulus comparison. However for the semantic versus prestimulus comparison, $Z > 2$ between 490ms and 590ms.

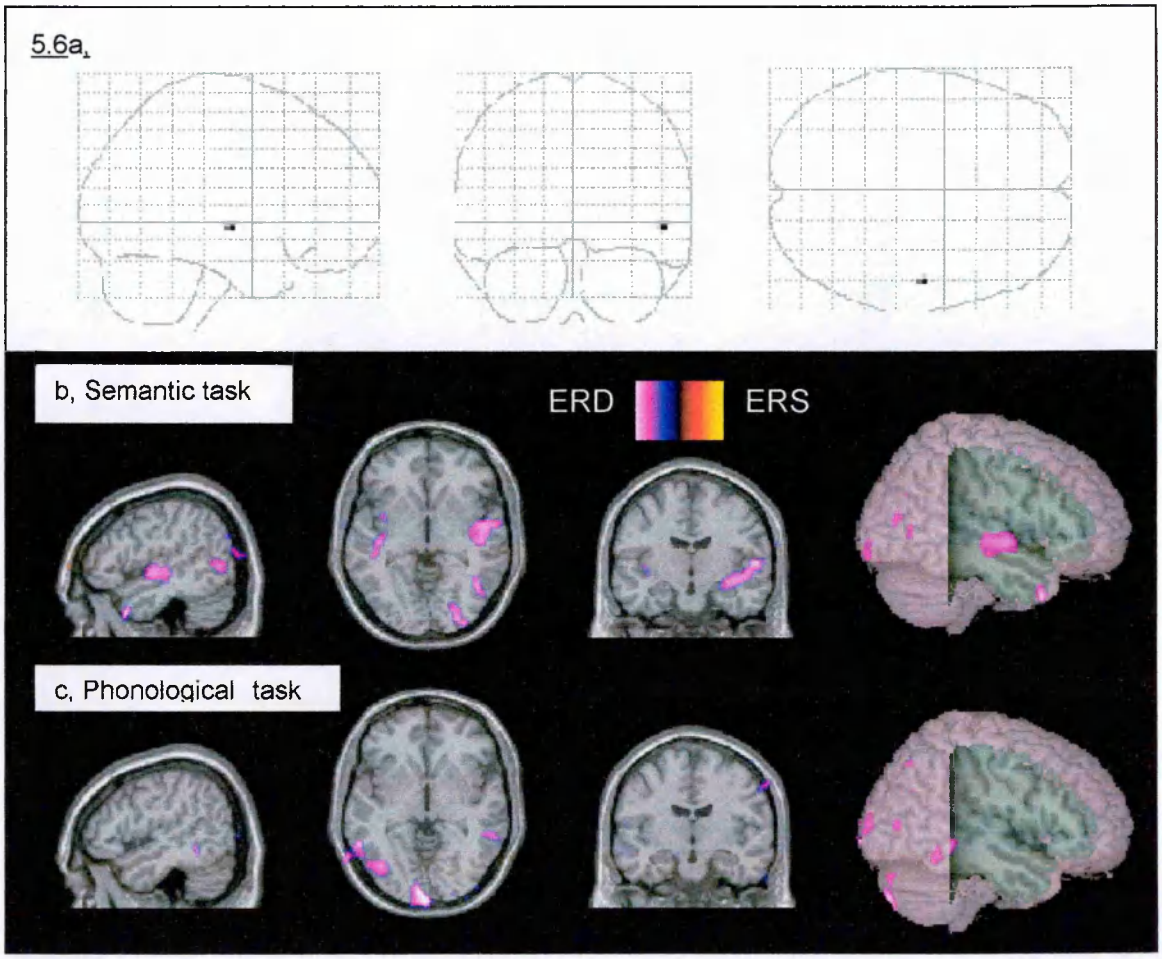


Figure 5.6, a) Glass brain images showing the location of the right superior temporal voxel identified within the 14-20Hz, 350-550ms semantic versus prestimulus comparison as showing statistically significant differential effects ($p<0.05$, talairach co-ordinates 51, -12, -3),

b) Group SAM rfx images for the 14-20Hz, 350-550ms semantic versus prestimulus comparison (where the right superior temporal voxel identified using SnPM was associated with a t value of -3.96), and

c) Group SAM rfx images for the 14-20Hz, 350-550ms phonological versus prestimulus comparison (where the same voxel was associated with a t value of 0.44). Both Group SAM images show values corresponding to $-3>t>3$.

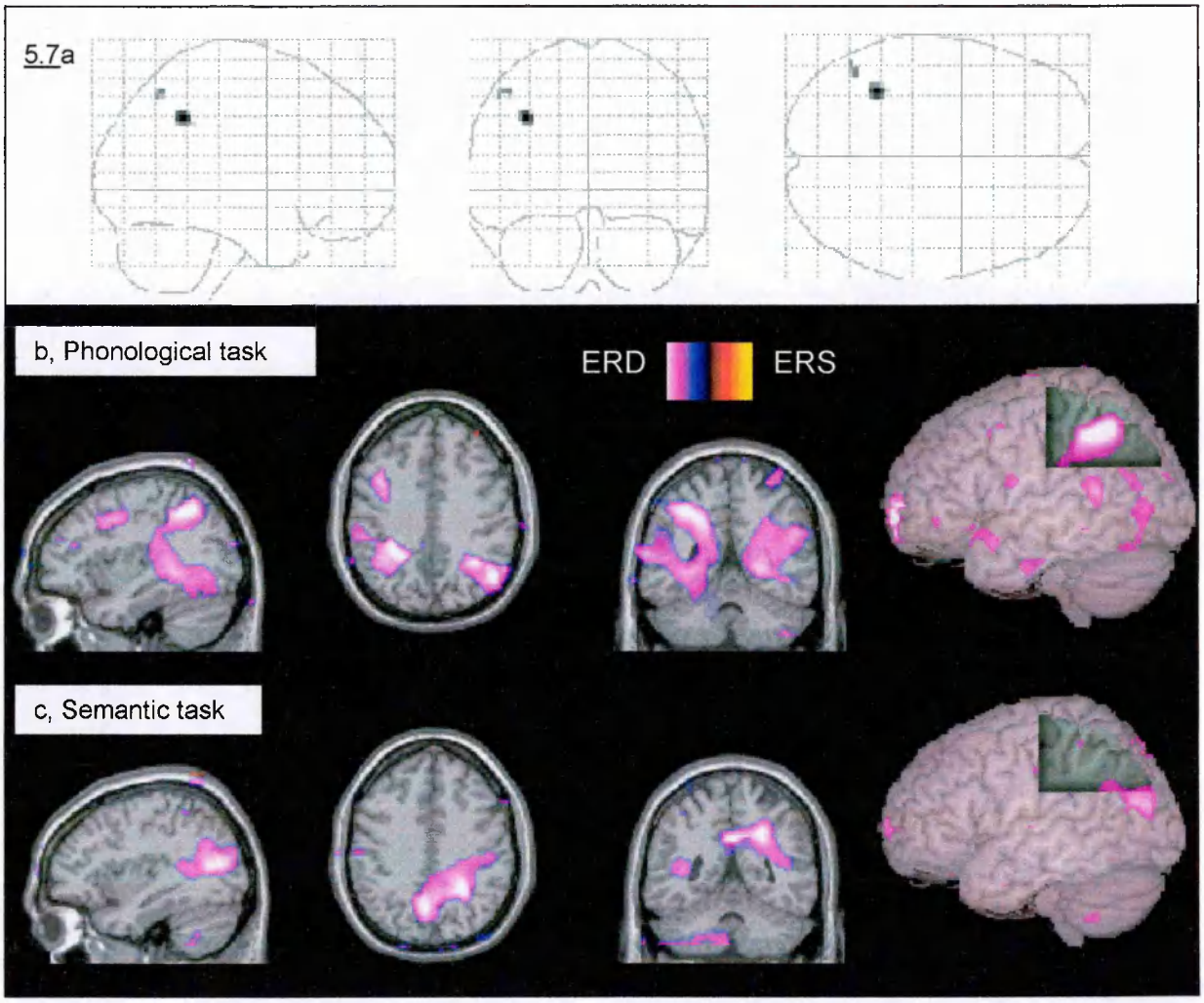


Figure 5.7. a) Glass brain images showing the location of the two left inferior parietal (BA40) voxels identified within the 20-30Hz, 350-550ms phonological versus prestimulus comparison as showing statistically significant differential effects ($p<0.05$, talairach co-ordinates –36, -48, 39, and –45, -60, 54).

b) Group SAM rfx images for the 20-30Hz, 350-550ms, phonological versus prestimulus comparison (where the voxel identified using SnPM was associated with a t value of -4.36).

c) Group SAM rfx images for the 20-30Hz, 350-550ms, semantic versus prestimulus comparison (where the same voxel was associated with a t value of –1.96). The images show values corresponding to $-3>t>3$.

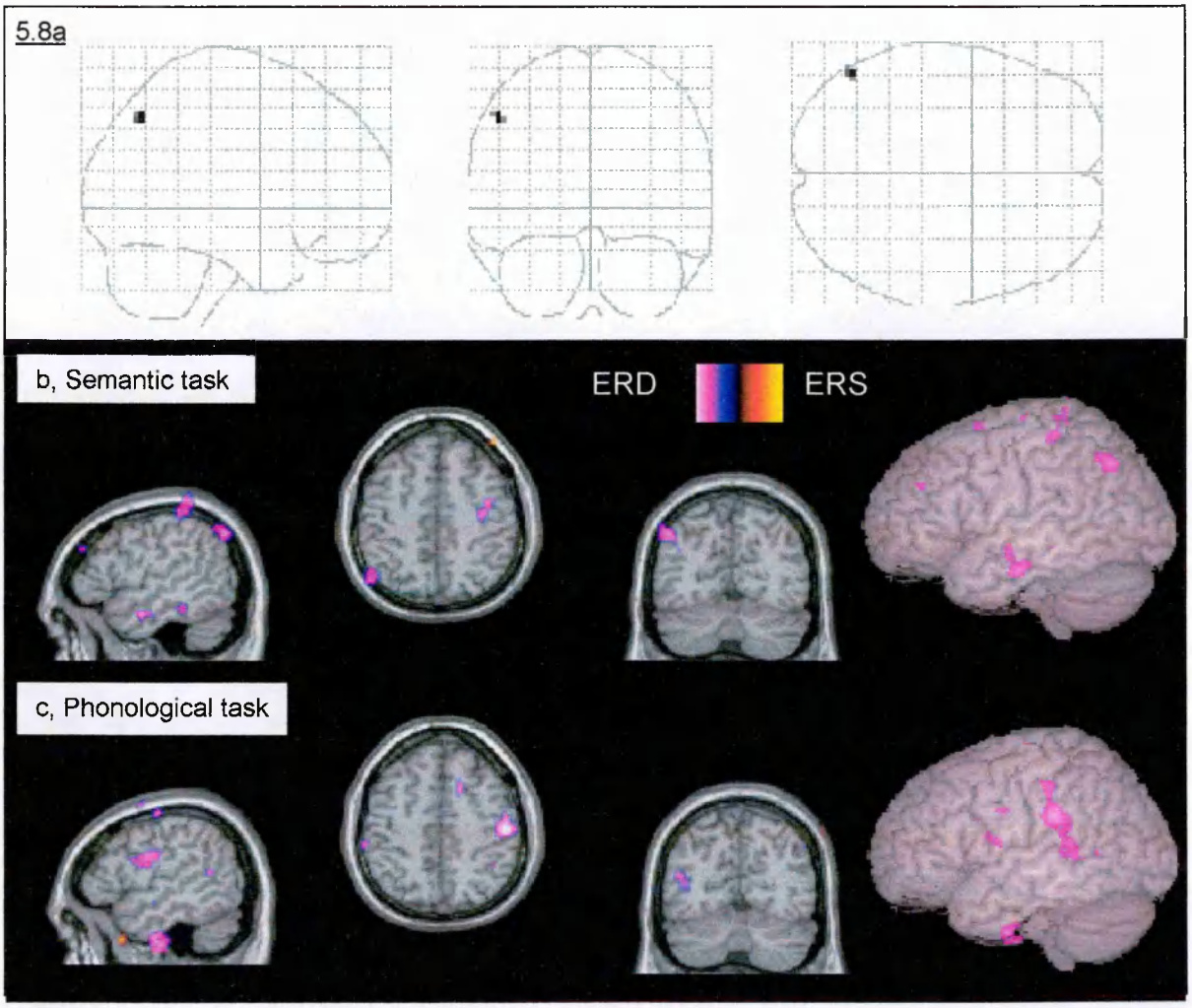


Figure 5.8, a) Glass brain images showing the location of the left inferior parietal (BA40) voxel identified within the 20-30Hz, 350-550ms, semantic versus prestimulus comparison (talairach co-ordinates –51, -66, 48),

b) Group SAM rfx images for the 20-30Hz, 500-700ms semantic versus prestimulus comparison (where the left inferior parietal (BA40) voxel identified using SnPM was associated with a t value of -3.71), and

c) Group SAM rfx images for the 20-30Hz, 500-700ms, phonological versus prestimulus comparison (where the same voxel was associated with a t value of -0.22). The images show values corresponding to –3>t>3.

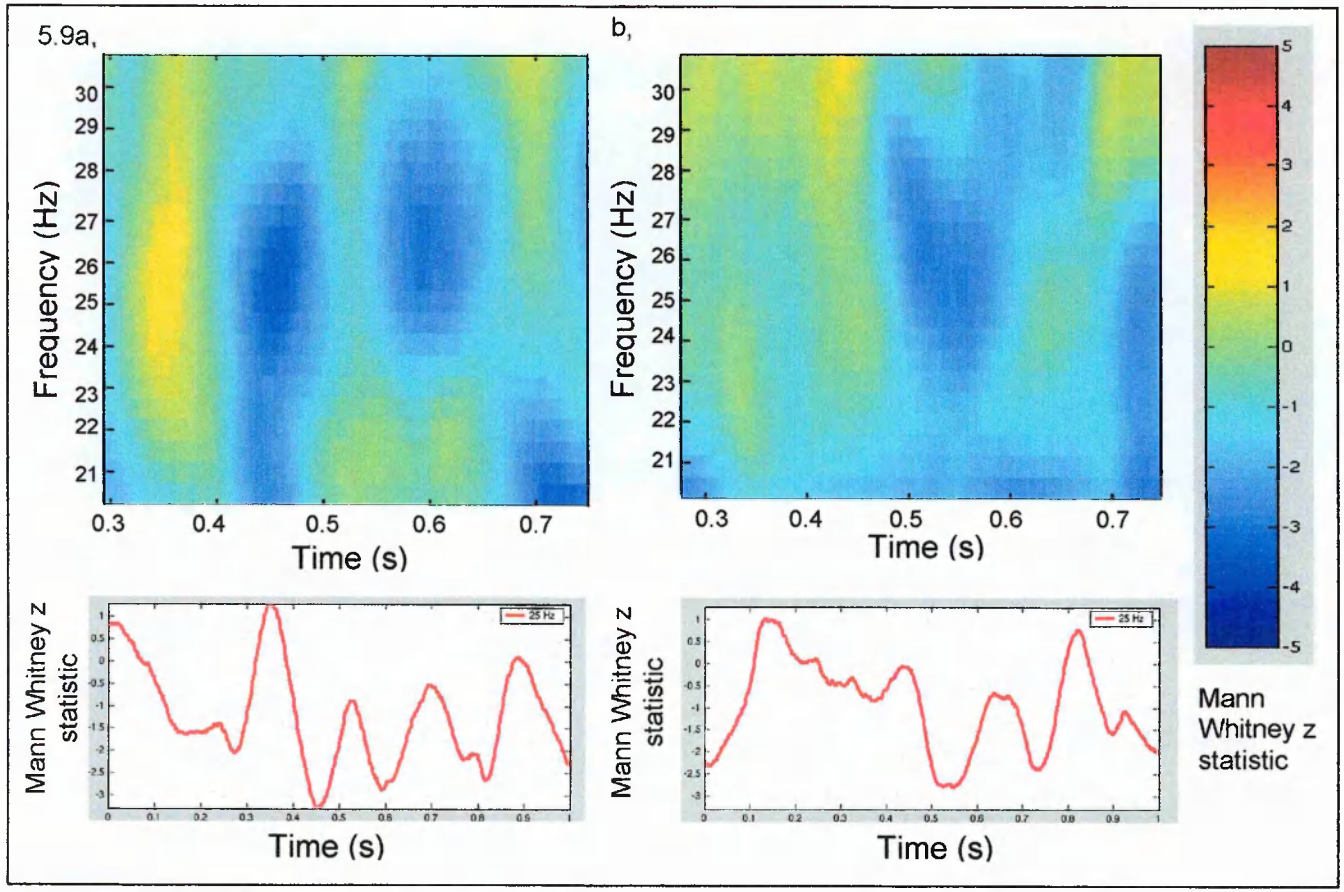


Figure 5.9, Example time-frequency Mann Whitney representation for

a) the phonological task versus prestimulus comparison, and

b) the semantic task versus prestimulus comparison, for a virtual electrode placed within BA40 of the left parietal lobe for one participant. The colour represents the Mann Whitney z statistic. The line graphs show the Mann Whitney Z statistic as a function of time for the 24Hz to 26Hz frequency band. A power decrease is observed within the beta frequency band at approximately 450ms after stimulus onset for the phonological task, but this occurs later for the semantic task.

5.7.5. Inferior frontal effects

Statistically significant ($p<0.05$) differential effects emerged within the phonological versus prestimulus comparison which were localised to the left inferior frontal gyrus (BA45) (figures 5.10), and observed within the 14-20Hz frequency band and the late 500-700ms time window.

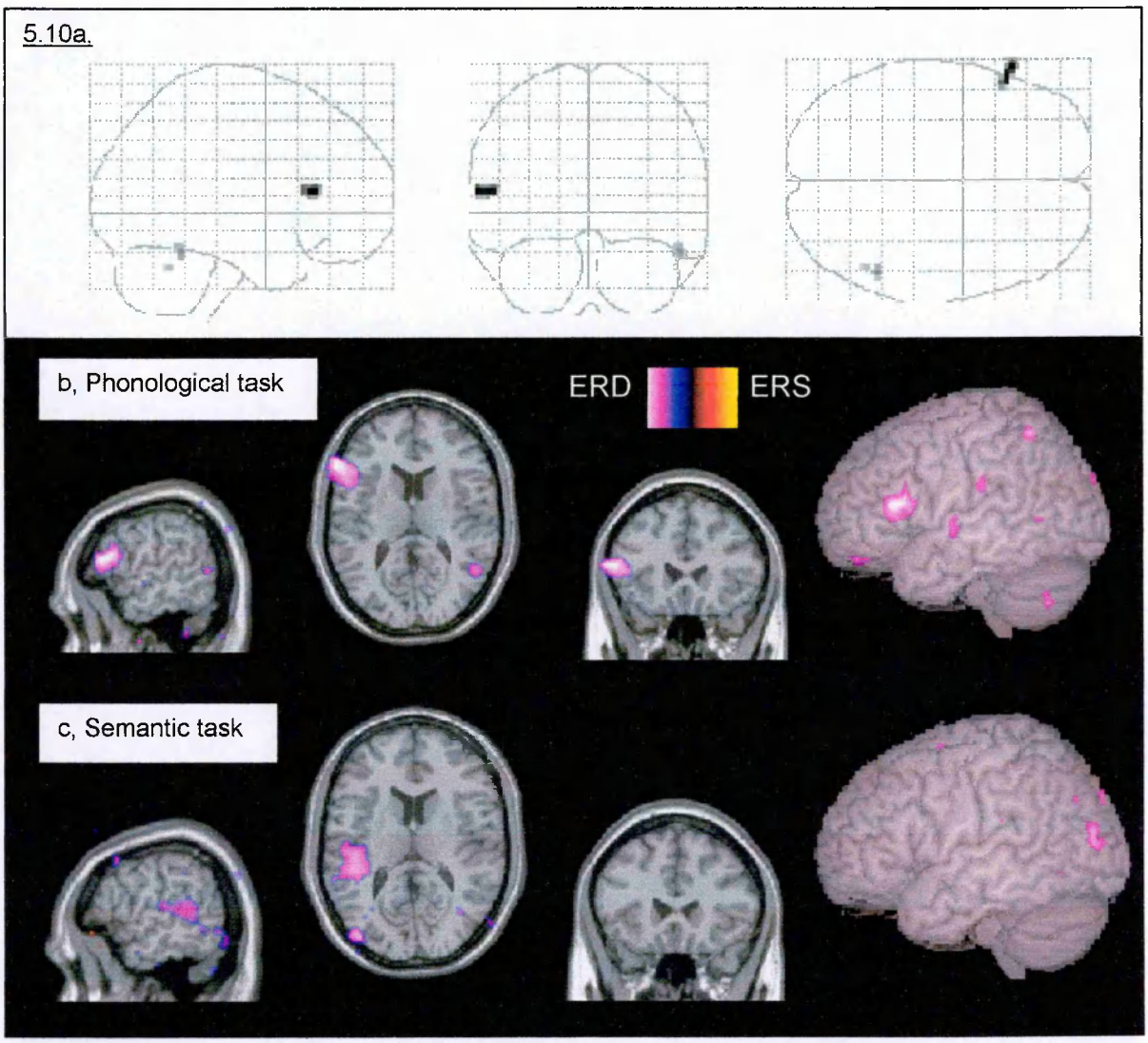


Figure 5.10. a) Glass brain images showing the location of the left inferior frontal voxel (in the region of BA45) identified within the 14-20Hz, 500-700ms phonological versus prestimulus comparison as showing statistically significant differential effects ($p<0.05$, talairach co-ordinates –57, 24, 12).

b) Group SAM rfx images for the 14-20Hz, 500-700ms phonological versus prestimulus comparison (where the left inferior frontal (BA45) voxel identified using SnPM was associated with a t value of –4.88), and

c) Group SAM rfx images for the 14-20Hz, 500-700ms semantic versus prestimulus comparison (where the same voxel was associated with a t value of –1.37). The images show values corresponding to $-3>t>3$.

An example Mann Whitney time-frequency representation for a virtual electrode placed within the left inferior frontal gyrus is shown in figure 5.11. This shows that in the case of this virtual electrode, and this individual, Z>2 (i.e. p<0.05) between 550ms and 700ms post stimulus onset.

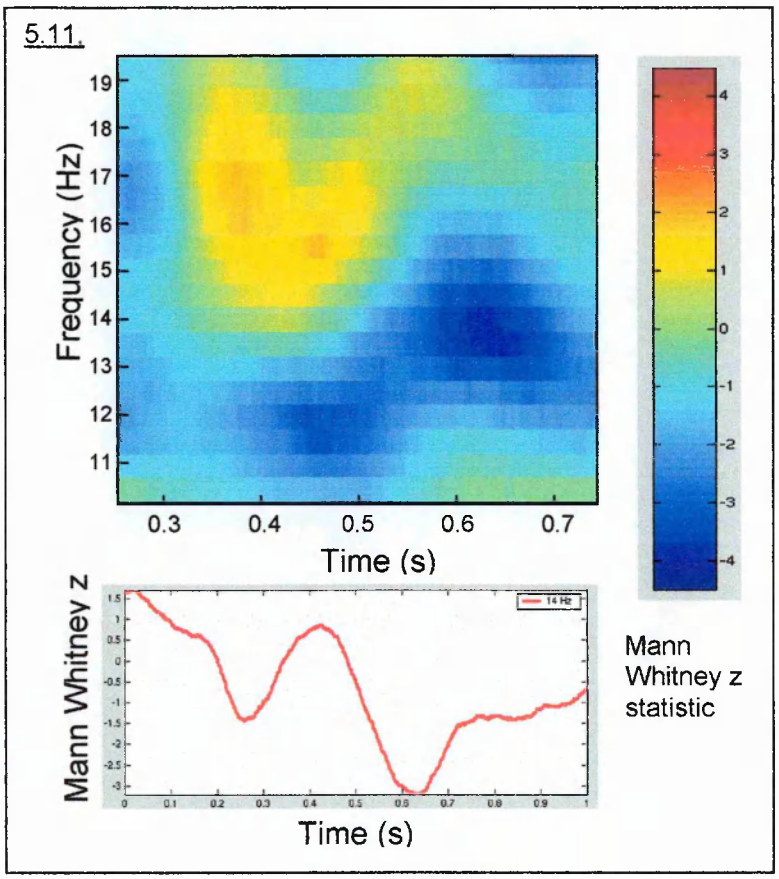


Figure 5.11. An example time-frequency Mann Whitney representation for a virtual electrode placed within the left inferior frontal gyrus for the 14-20Hz, 500-700ms, phonological task versus prestimulus comparison. A power decrease is observed within the low beta frequency band (approximately 14Hz) at approximately 600ms after stimulus onset. The colour represents the Mann Whitney Z statistic. The line graph shows the Mann Whitney z statistic as a function of time for the 13Hz to 15Hz frequency band.

Individual normalised SAM images also showed left inferior frontal peaks within the semantic versus prestimulus comparison (figure 5.12). Although this effect did not reach significance at the group level, maybe due to individual variations in the location of these effects and the frequency band in which they were observed, five participants showed peaks of T>2 within the left inferior frontal gyrus in the 500-700ms time window. These peaks emerged within the 30-40Hz frequency band for four of the participants, the 20-30Hz band for one participant. All of the peaks that fulfilled the T>2 criteria were left lateralised.

An example Mann Whitney time-frequency representation for the semantic task versus prestimulus comparison, for a virtual electrode placed within the left inferior frontal gyrus in the region of BA47, shows a power decrease within the beta frequency range at approximately 350-550ms post stimulus onset (figure 5.13).

5.7.6, Right frontal precentral effects

Right frontal precentral ERD also reached significance ($p<0.05$) at the group level within the phonological versus prestimulus 350-550ms, 30-40Hz comparison (figure 5.14). An example Mann Whitney representation for a virtual electrode placed within the right frontal precentral gyrus (BA44) is presented in figure 5.15, and shows a power decrease with low beta frequency band at approximately 550-700ms, in the phonological task condition.

5.12.

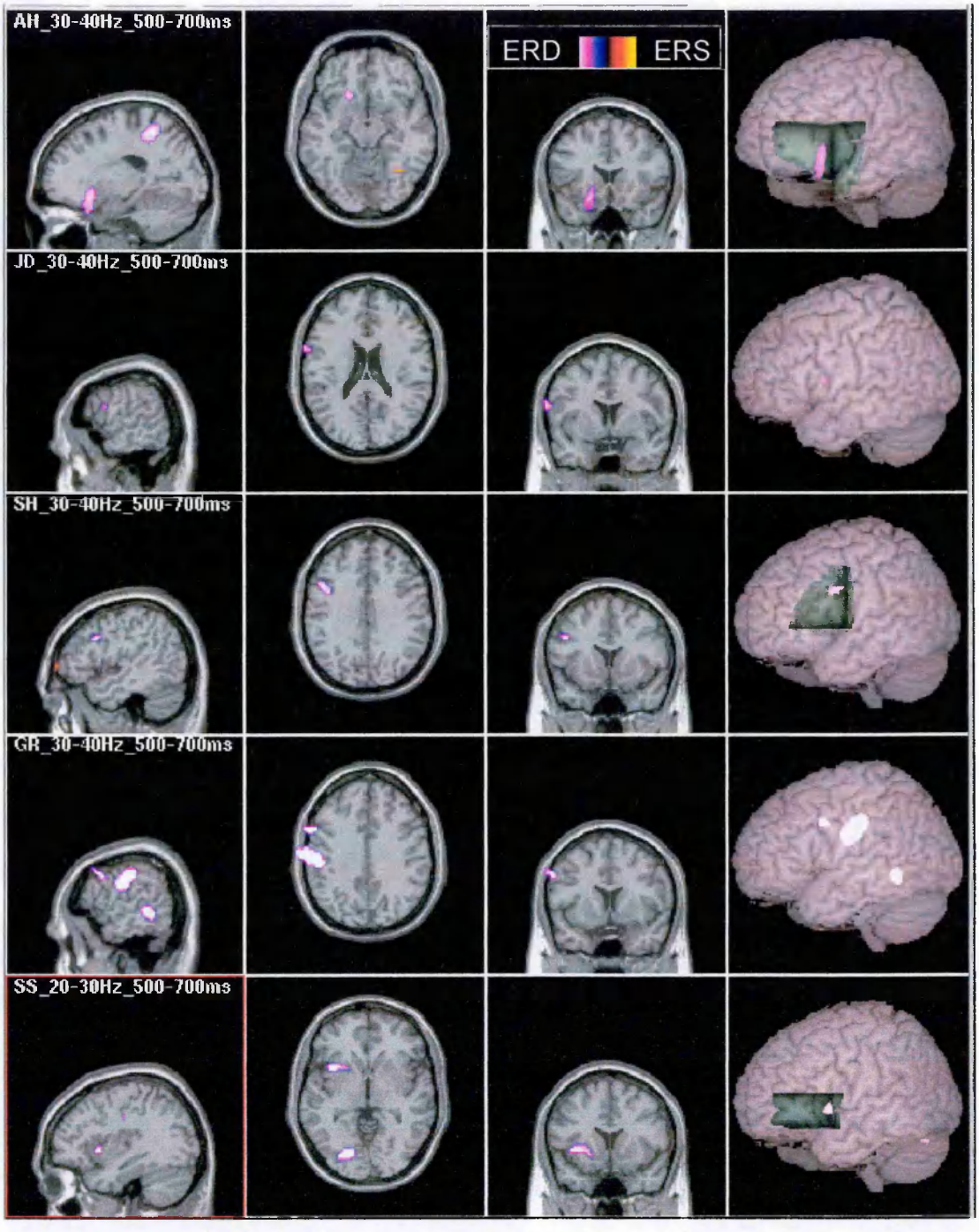


Figure 5.12. Normalised SAM images for individual participants showing peak t values of t<-2 in the region of the left inferior frontal gyrus. Within the 500-700ms time window, peaks were observed within both the 20-30Hz and 30-40Hz frequency bands for the semantic task versus prestimulus comparison. The location of the peaks also varied from BA44/47 to BA9. A threshold of t<-2 has been applied.

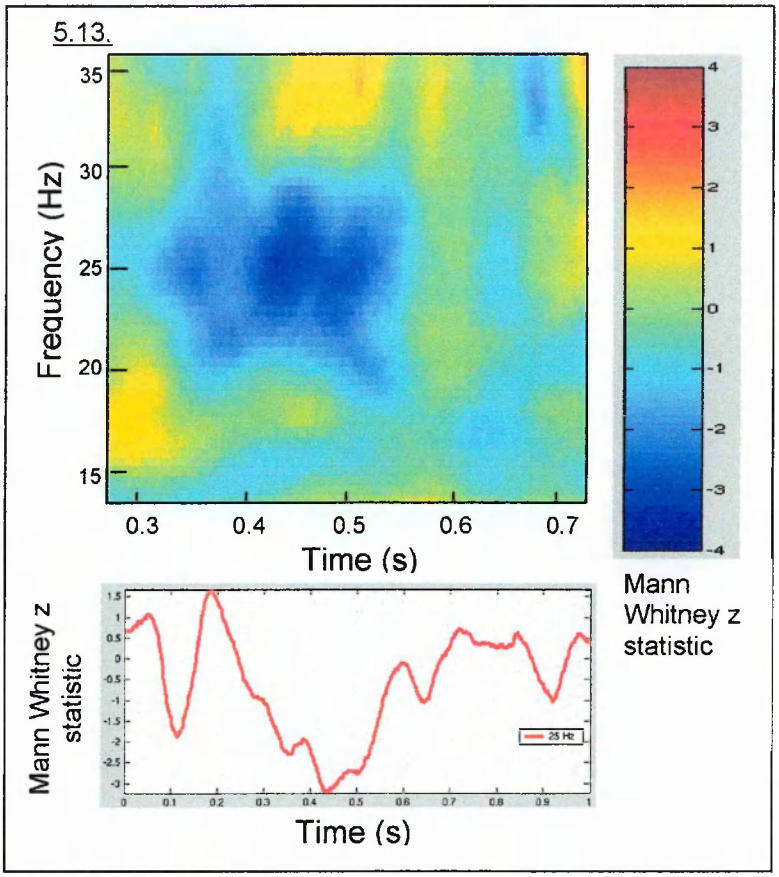


Figure 5.13. An example time-frequency Mann Whitney representation for the semantic task versus prestimulus comparison for a virtual electrode placed within the left inferior frontal gyrus (BA47). A power decrease is observed within the beta frequency band (approximately 25Hz) at approximately 450ms after stimulus onset. The colour represents the Mann Whitney z statistic. The line graph shows the Mann Whitney z statistic as a function of time for the 24Hz to 26Hz frequency band. $Z>2$ (corresponding to $p<0.05$) between approximately 350 and 550ms after stimulus onset.

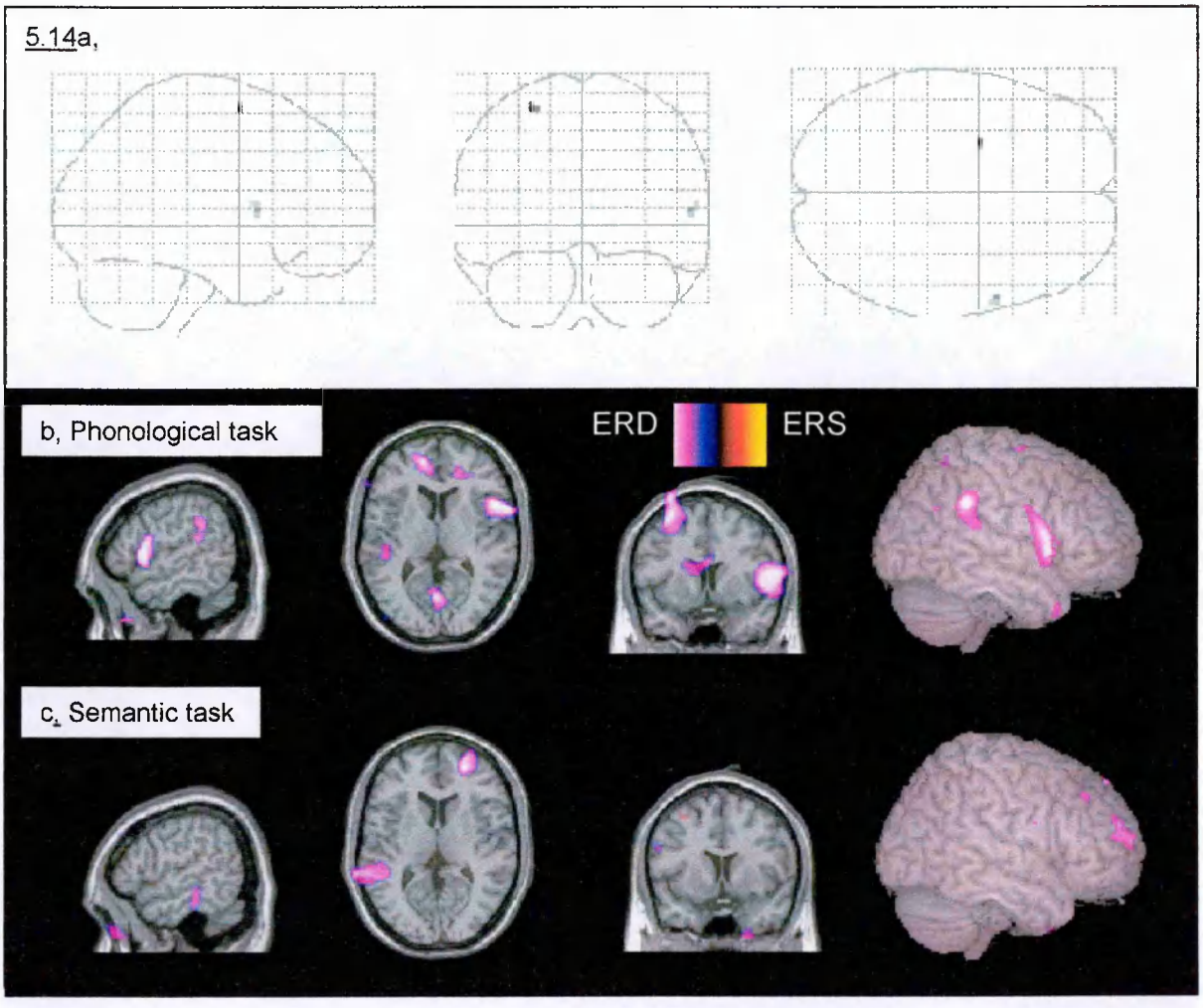


Figure 5.14, a) Glass brain images showing the location of the right precentral frontal voxel (BA44) identified within the 30-40Hz, 350-550ms phonological versus prestimulus comparison as showing statistically significant differential effects ($p<0.05$, talairach co-ordinates 57, 9, 9).

b) Group SAM rfx images for the 30-40Hz, 350-550ms, phonological versus prestimulus comparison (where the right frontal precentral gyrus (BA44) voxel identified using SnPM was associated with a t value of –5.21), and

c) Group SAM rfx images for the 30-40Hz, 350-550ms, semantic versus prestimulus comparison (where the same voxel was associated with a t value of 0.76). The images show values corresponding to $-3>t>3$.

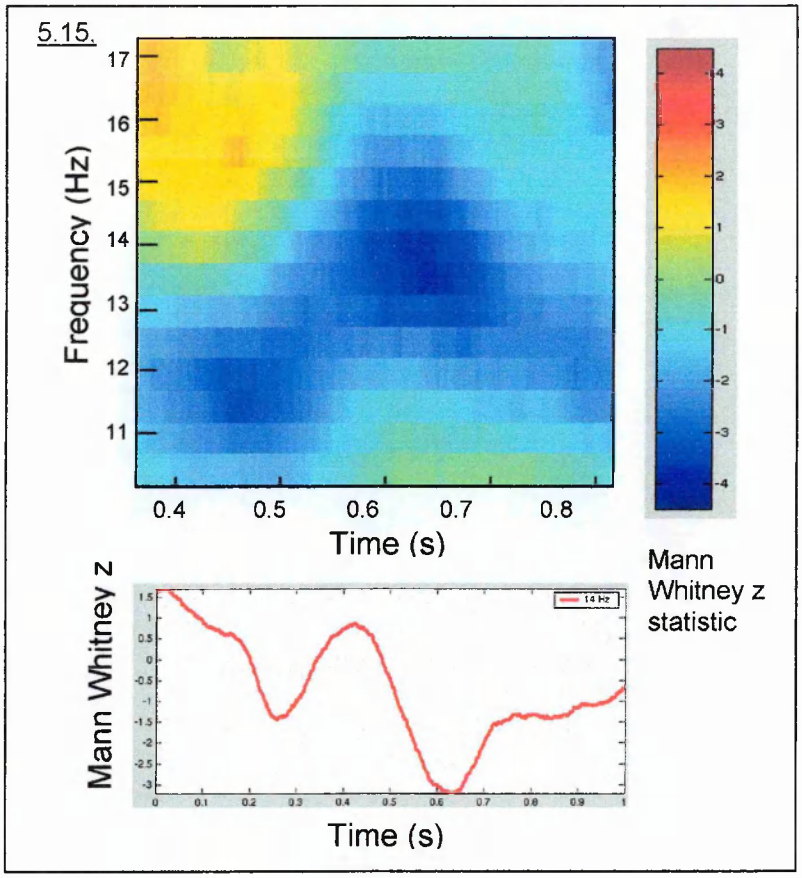


Figure 5.15. An example time-frequency Mann Whitney representation for the phonological task versus prestimulus comparison for a virtual electrode placed within the right frontal precentral gyrus (BA44) for one participant. A power decrease is observed within the low beta frequency band. The colour represents the Mann Whitney z statistic. The line graph shows the Mann Whitney z statistic as a function of time for the 13Hz to 15Hz frequency band. $Z>2$ (corresponding to $p<0.05$) between approximately 550 and 700ms after stimulus onset.

5.7.7. Superior / middle frontal effects (BA10)

Both semantic (figure 5.16) and phonological (figure 5.17) task comparisons revealed statistically significant event-related desynchronisation ($p<0.05$) within BA10 of the left superior/middle frontal regions. These effects were confined to the gamma frequency range (30-40Hz in the case of the phonological task, and 40-50Hz in the case of the semantic task). The semantic effect emerged earlier (350-550ms) than the phonological effect (500-700ms).

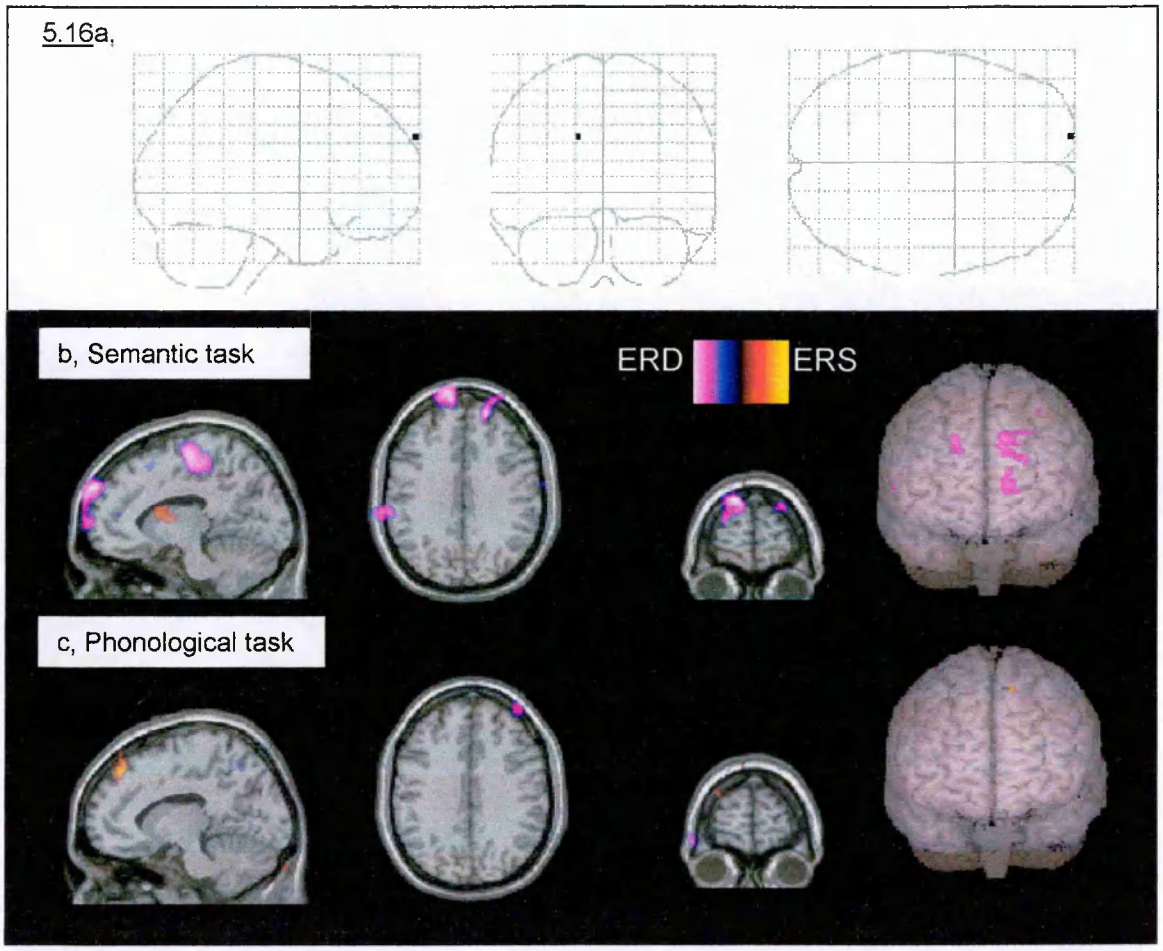


Figure 5.16, a) Glass brain images showing the location of the left superior frontal voxel (in the region of BA10) identified in the 40-50Hz, 350-550ms semantic versus prestimulus comparison ($p<0.05$, talairach co-ordinates –15, 69, 33),

b) Group SAM rfx images for the 40-50Hz, 350-550ms, semantic versus prestimulus comparison (where the left superior frontal (BA10) voxel identified using SnPM was associated with a t value of –3.94), and

c) Group SAM rfx images for the 40-50Hz, 350-550ms, phonological versus prestimulus comparison (where the same voxel was associated with a t value of 2.10). The images show values corresponding to $-3>t>3$.

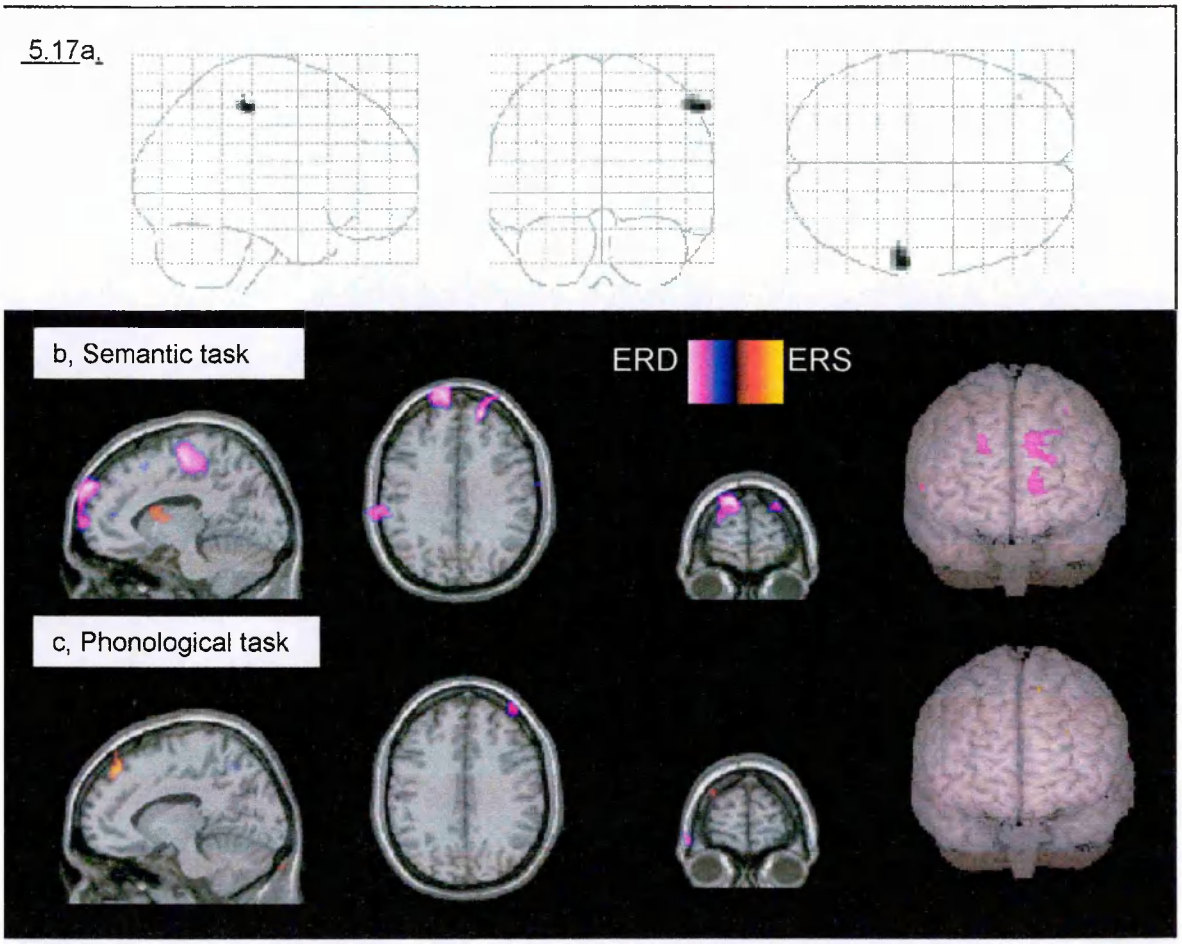


Figure 5.17. a) Glass brain images showing the location of the left superior / middle frontal voxel (in the region of BA10) identified in the 30-40Hz, 500-700ms phonological versus prestimulus comparison ($p<0.05$, talairach co-ordinates –39, 39, 30).

b) Group SAM rfx images for the 30-40Hz, 500-700ms, phonological versus prestimulus comparison (where the left middle frontal (BA10) voxel identified using SnPM was associated with a t value of –4.31), and

c) Group SAM rfx images for the 30-40Hz, 500-700ms, semantic versus prestimulus comparison (where the same voxel was associated with a t value of –0.96). The images show values corresponding to $-3>t>3$.

An example Mann Whitney representation for the semantic versus prestimulus comparison for a virtual electrode placed within left BA10 in one participant is presented in figure 5.18. This shows a power decrease within the gamma frequency range at approximately 500ms post stimulus onset.

An example Mann Whitney representation for the phonological versus prestimulus comparison for a virtual electrode placed within left BA10 in one participant is presented in figure 5.19. This also shows a power decrease within the gamma frequency range, although this occurs later, in this case at approximately 750ms post stimulus onset.

5.7.8, Cerebellar effects

The phonological task, but not the semantic task, was associated with statistically significant event-related desynchronisation located within right cerebellar voxels, within the 14-20Hz frequency band, and within both the 350-550ms and 500-700ms time windows ($p<0.05$) (figures 5.20 and 5.21).

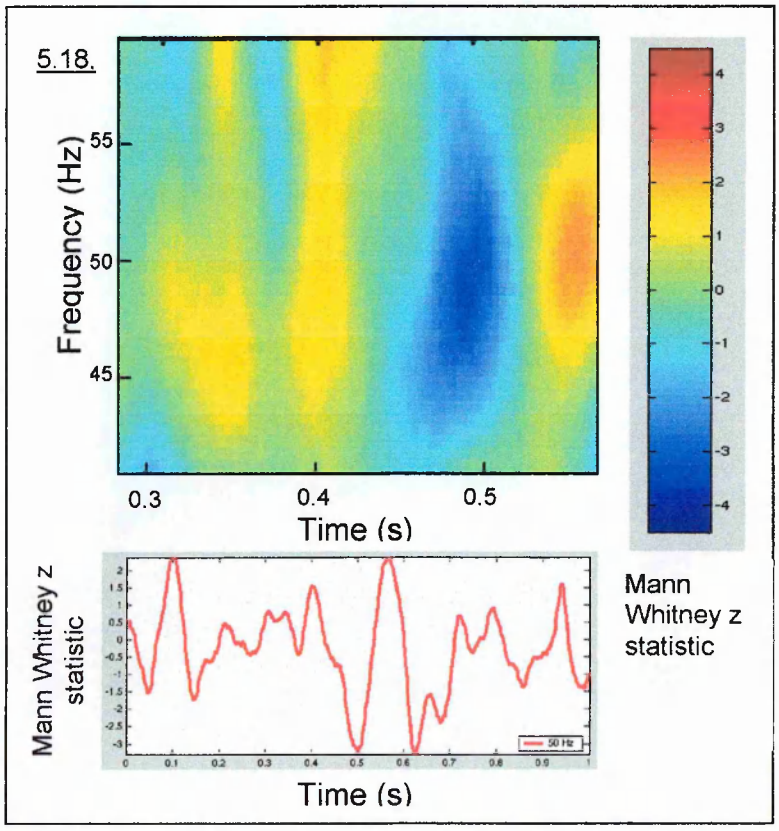


Figure 5.18. An example time-frequency Mann Whitney representation for the semantic task versus prestimulus comparison for a virtual electrode placed within the left middle frontal gyrus (BA10) for one participant. A power decrease is observed within the gamma frequency band. The colour represents the Mann Whitney z statistic. The line graph shows the Mann Whitney z statistic as a function of time for the 49Hz to 51Hz frequency band. Z>2 (corresponding to $p<0.05$) between approximately 450 and 700ms after stimulus onset.

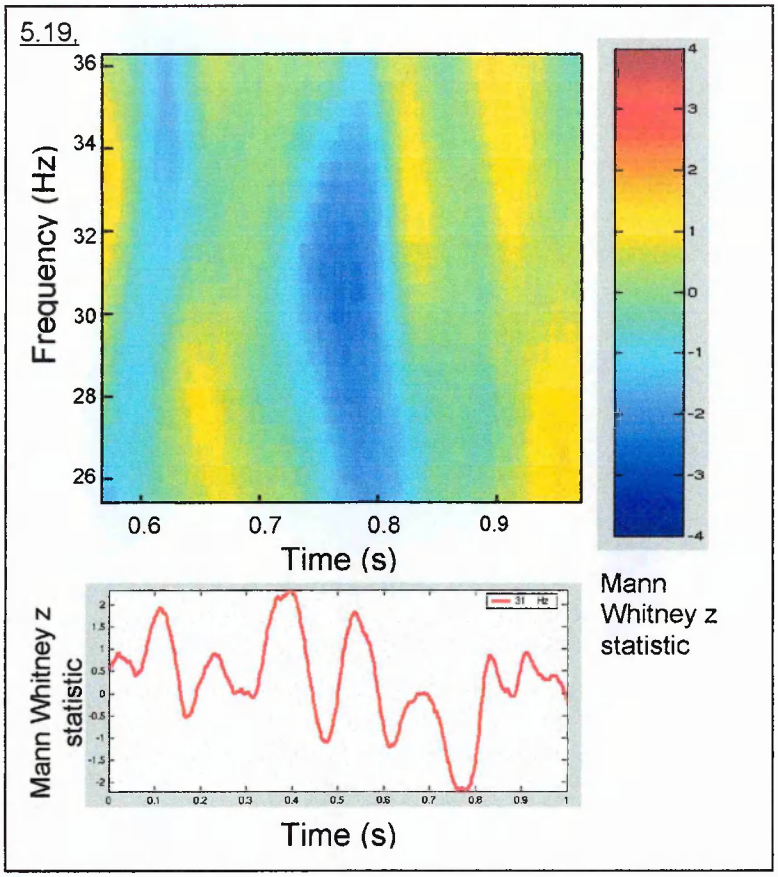


Figure 5.19. An example time-frequency Mann Whitney representation for the phonological task versus prestimulus comparison for a virtual electrode placed within the left superior frontal gyrus (BA10) for one participant. A power decrease is observed within the gamma frequency band. The colour represents the Mann Whitney z statistic. The line graph shows the Mann Whitney z statistic as a function of time for the 30Hz to 32Hz frequency band. $Z>2$ (corresponding to $p<0.05$) between approximately 750 and 800ms after stimulus onset.

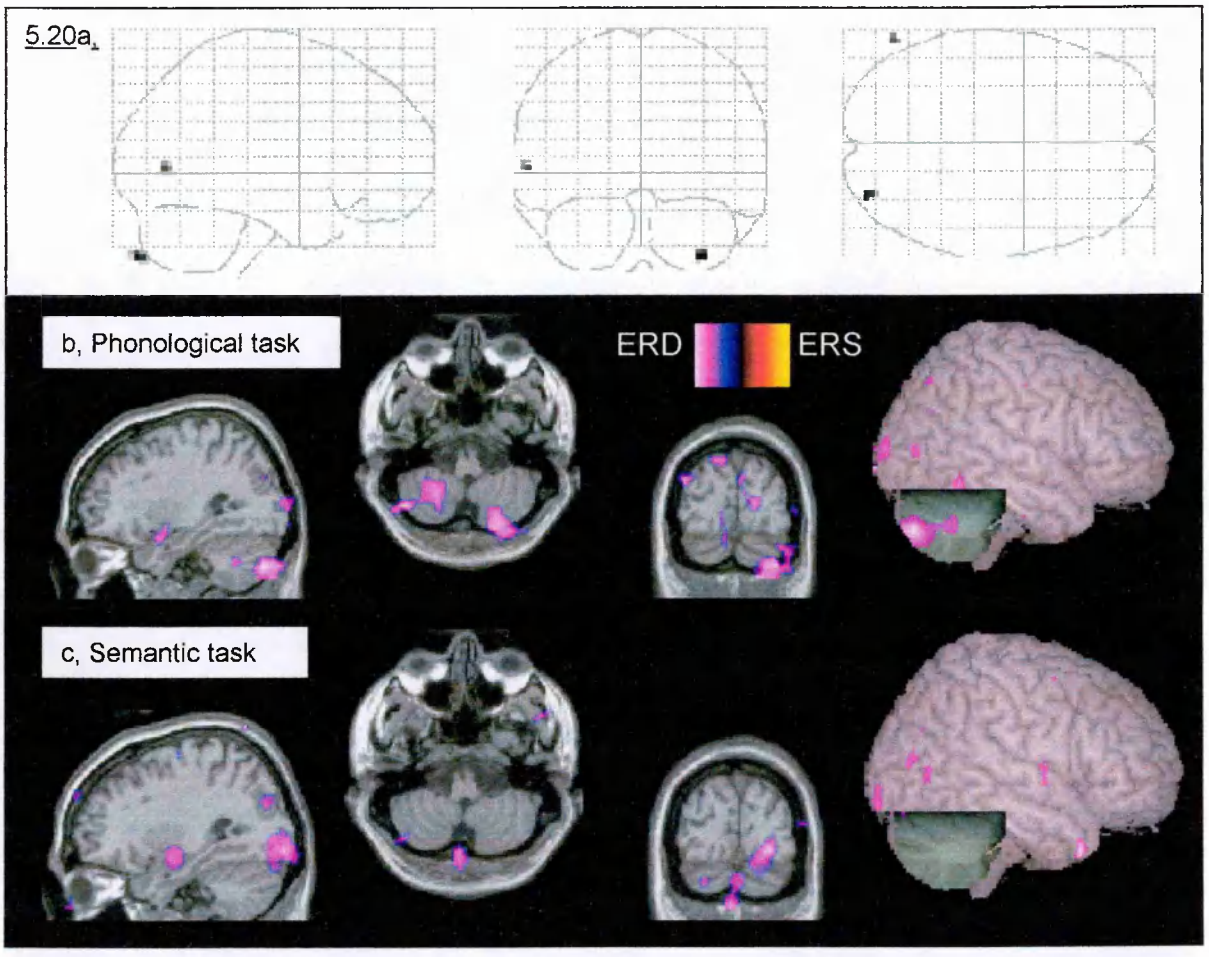


Figure 5.20, a) Glass brain images showing the location of the right cerebellar voxels identified within the 14-20Hz, 350-550ms, phonological versus prestimulus comparison as showing statistically significant differential effects ($p<0.05$, talairach co-ordinates 30, -87, -48),

b) Group SAM rfx images for the 14-20Hz, 350-550ms, phonological versus prestimulus comparison (where the right cerebellar voxel identified using SnPM was associated with a t value of –3.96), and

c) Group SAM rfx images for the 14-20Hz, 350-550ms, semantic versus prestimulus comparison (where the significant voxel was associated with a t value of –1.37). The images show values corresponding to $-3>t>3$.

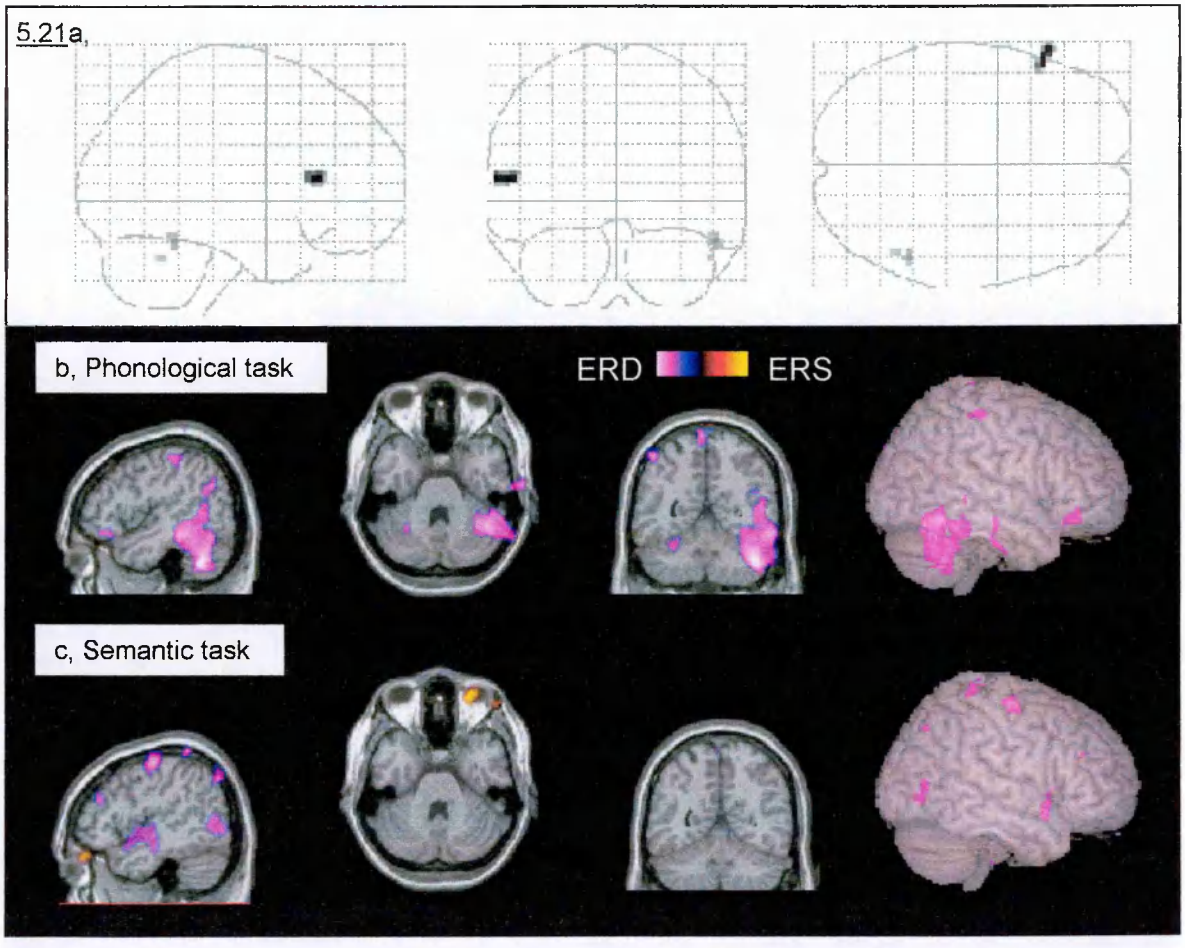


Figure 5.21, a) Glass brain images showing the location of the right cerebellar voxels identified within the 14-20Hz, 500-700ms, phonological versus prestimulus comparison as showing statistically significant differential effects ($p<0.05$, talairach co-ordinates 48, -54, -30),

b) Group SAM rfx images for the 14-20Hz, 500-700ms phonological versus prestimulus comparison (where the right cerebellar voxel identified using SnPM was associated with a t value of –4.13), and

c) Group SAM rfx images for the 14-20Hz, 500-700ms, semantic versus prestimulus comparison (where the significant voxel was associated with a t value of –0.50). The images show values corresponding to $-3>t>3$.

An example Mann Whitney representation for the phonological versus prestimulus comparison for a virtual electrode placed within the right cerebellum in one participant is presented in figure 5.22. This also shows a power decrease within the beta frequency range, at approximately 450ms post stimulus onset.

Although cerebellar differential effects observed within the semantic versus prestimulus comparison failed to reach statistical significance at the group level, seven participants showed peaks of t>2. There appeared to be a high degree of individual variability relating to the time window and frequency bands in which these effects were observed.

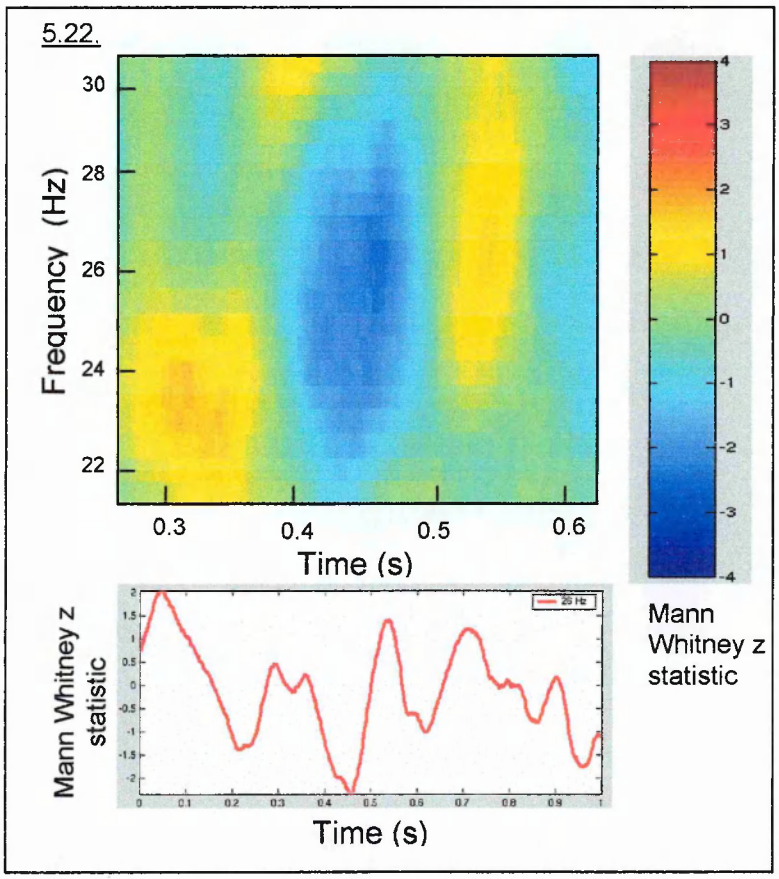


Figure 5.22, An example time-frequency Mann Whitney representation for the phonological task versus prestimulus comparison for a virtual electrode placed within the right cerebellum for one participant. A power decrease is observed within the beta frequency band. The colour represents the Mann Whitney z statistic. The line graph shows the Mann Whitney z statistic as a function of time for the 25Hz to 27Hz frequency band. Z>2 (corresponding to p<0.05) at approximately 450ms after stimulus onset.

5.7.9. Spatial-temporal dynamics within the semantic task condition

In order to investigate the relative latencies of left temporal and left inferior frontal semantic task effects, the data from the five participants who showed ERD peaks of T>2 at both left temporal and left inferior frontal locations were subjected to further analysis. Virtual electrodes were placed at these locations, and from Mann Whitney time-frequency representations, latencies were identified at which Z>2 ($p<0.05$). These latencies, presented in figure 5.23, show that for four out the five participants, such left frontal effects preceded the left temporal effects.

5.23.

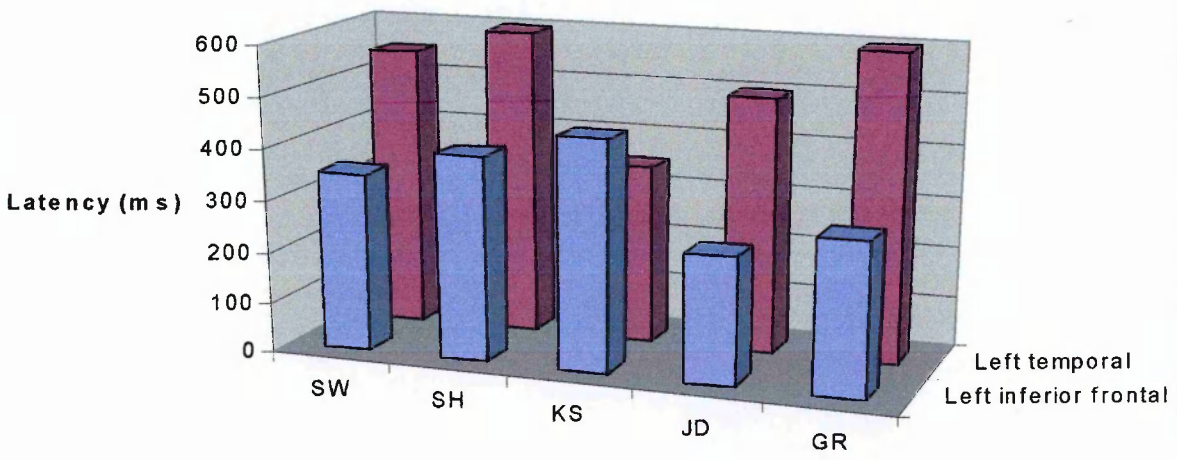


Figure 5.23. Five participants showed peak T values of t>2 both within the left temporal lobe and left inferior frontal regions (BA46/47). Virtual electrodes were placed at these locations, and based upon time-frequency Mann Whitney representations, latencies were identified at which Mann Whitney Z> 2 (i.e. $p<0.05$). These latencies are presented for each of the five participants, showing that for four of these participants the left inferior frontal ERD preceded the left temporal ERD.

As statistically significant left temporal and left frontal BA10 ERD was identified within the same time window (350-550ms), in the semantic task conditions, further analysis was conducted in order to investigate the latencies of these two effects. Three participants were identified in which ERD peaks of T>2 were identified within both the left temporal lobe, and the left frontal regions corresponding to the BA10 voxel identified using SnPM analysis. Virtual electrodes were placed at these locations, and using Mann Whitney time-frequency representations, latencies were identified at which Z>2. These

latencies are displayed in figure 5.24. In each of these cases the left frontal (BA10) effects preceded the left temporal effects.

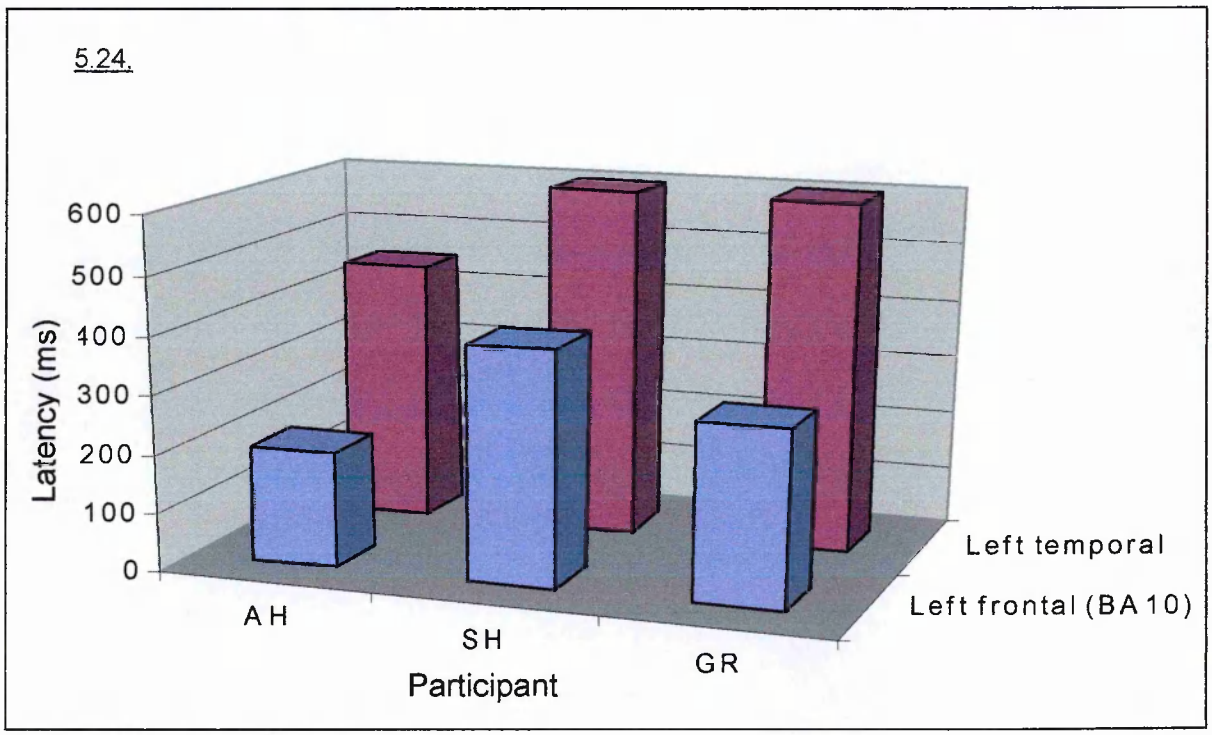


Figure 5.24. Three participants showed peak T values of t>2 both within the left temporal lobe and the left frontal regions coinciding with the BA10 voxel identified from SnPM analysis. Virtual electrodes were placed at these locations, and based upon time-frequency Mann Whitney representations, latencies were identified at which Mann Whitney Z> 2 (i.e. $p<0.05$). These latencies are presented for each of the three participants, showing that in each of these cases the left frontal ERD preceded the left temporal ERD.

5.8, MEG Study: Conclusion

As anticipated, there was no significant difference in the level of accuracy with which the two task conditions were completed, suggesting that the tasks were similar in terms of difficulty. It should be noted that reation times were not collected within this study as a cued response was used, in an attempt to reduce confounds associated with response initiation occurring at the the same time as stimulus processing. As discussed in section 4.2, syllable counting tasks have tended to be associated with longer reaction times compared to various semantic decision tasks, such as making matching words according to the colour or typical location of their referents (Mummery et al 1998). It therefore seems reasonable to assume that had the paradigm allowed the measurement of reaction times, the phonological task would have been associated with longer reaction times than the semantic task. Although this difference may have obscured the results of semantic v phonological comparisons (which in this study failed to reach statistical significance), by considering each condition with respect to the prestimulus baseline, it was possible to investigate semantic and phonological effects separately and avoid any confounds associated with reaction time differences between conditions.

Although individual normalised SAM images for both of the task conditions compared to the prestimulus baseline show a degree of intersubject variability within each of the three domains (space, time and frequency), networks of voxels were identified in which significant differential effects emerged at the group level. Each of these effects arose from enhanced ERD associated with the task condition compared to the prestimulus interval. Although there were staticistically significant effects ($p<0.05$) observed with each of the two task conditions compared to the presetimulus baseline, differential effects observed within the semantic v phonological comparisons failed to reach statistical significance ($p<0.05$) at the group level. As there was no reason to believe that there were differences between the prestimulus baseline used in each of the task comparisons, this implies that when a significant effect was observed within one of the two task conditions, a similar, but sub-theshold, effect was associated with the other task condition. This also seems reasonable considering behavioural findings that suggest an involvement of implict semantic processing within phonological task conditions, and vice versa (as discussed in section 4.2.2). The following discussion therefore considers the results of semantic and phonological task conditions with respect to the prestimulus baseline.

5.8.1, Frequency effects

Irrespective of the task condition, group level temporal, parietal, inferior frontal and cerebellar differential effects were confined to the beta frequency range (14-20Hz and 20-30Hz, with the only exception being right precentral effects associated with the phonological task which emerged within the 30-40Hz frequency band). These regions have often been identified as contributing to semantic and phonological "networks". The finding that these temporal, parietal, inferior frontal and cerebellar effects occur within the beta range may further support the claim that these regions may be "working together", and show large scale synchronization believed to be necessary for language processing (Weiss & Mueller, 2003).

Besides the beta effects, both of the task conditions were also associated with enhanced ERD within BA10 of the left superior/middle frontal gyrus in the gamma frequency range (30-40Hz and 40-50Hz). The frequency dissociation between these effects and those observed within the other regions may support the hypothesis that superior/middle frontal regions (in particular BA10) may play a different role, such as reasoning and integration (Christoff et. al. 2001).

5.8.2, Temporal effects

Contrary to other studies (e.g. Mummery et. al. 1998), this study failed to identify inferior temporal effects that were statistically significant at the group level within the semantic task condition. However, peak t values were identified within inferior temporal regions within individual participants. It seems likely that spatial variability may have prevented these peaks from producing a significant effect at the group level. Appendix 4.1 indicates that there is a high degree of variability between the inferior temporal regions identified within previous imaging studies. Suggestions that the involvement of inferior temporal regions may be influenced by category specific effects (Pulvermuller, 2001) and differences in the nature of semantic associations (Mummery et. al. 1998) would also imply that these regions may be particularly susceptible to individual differences.

5.8.3, Middle temporal / temporo-parietal effects

In keeping with the suggestion that the left temporo-parietal-occipital junction (BA39), and in particular the angular gyrus, may play a role linked to semantic processing

(Price, 2000), statistically significant ERD was identified within two voxels in this region for the semantic task condition. Within the phonological task condition, statistically significant ERD was identified within one voxel, which was inferior to those voxels identified within the semantic condition, and bordered the occipital lobe (BA37).

Should these effects reflect the involvement of the same region in both task conditions, this raises the possibility that the findings either support the original claim that BA39 and the angular gyrus may act as a "visual word form area", which fails to differentiate between semantic and nonsemantic processing. Alternatively, the involvement of this region within the phonological task condition may result from implicit semantic processing, which would be plausible from the findings of behavioral studies (Gabrieli et. al. 1998).

It is also possible that these effects originate from different regions. The ERD observed within the phonological task condition lies at the border between occipital and temporal lobes. It therefore seems reasonable to speculate that this effect may be associated with lower level visual analysis, which, based upon previous reaction time results (Mummery et. al. 1998), may be more sustained within the phonological condition.

5.8.4, Fusiform effects

Statistically significant fusiform effects failed to emerge at the group level for either of the two task conditions, in line with the findings of Roskies et. al. (2001). Roskies et. al. speculate that their absence of significant task related differential effects may have resulted from implicit semantic processing within their phonological condition. It seems unlikely that this was the case within this study, as no group level significant task-related fusiform effects emerged, even when the prestimulus time was used as a baseline. Roskies et. al. also suggest that semantic systems within this region may be so widely distributed that the diffuse activity remains subthreshold, which may also have applied to the present study.

5.8.5, Parietal effects

Although statistically significant ERD was observed within BA40 of the left inferior parietal lobule for both of the tasks compared to their prestimulus interval, there were differences between the results obtained from the two conditions. Statistically

significant ERD emerged earlier within the phonological task condition (350-550ms) than within the semantic task condition (500-700ms). The earlier recruitment of this region within the phonological task condition would fit with previous accounts of this region representing a "phonological store". The later involvement of this region within the semantic task may be consistent with behavioral reports of implicit phonological processing occurring within semantic task conditions (Van Orden et. al. 1988). Although, within this behavioral study implicit phonological processing was thought to account for phonologically driven false alarms in a category decision task, suggesting that the phonological processing may have preceded the semantic response. However, it seems likely that other factors would need to be considered, such as the type of words read (Price et. al. 1999), and possibly the relative familiarity of the auditory and visual representation of the words used.

The BA40 effects observed within this study were left lateralised, although bilateral effects have been reported previously. The reports have tended to be based on PET and fMRI findings (for example, Mummery et. al. 1998; McDermott et. al. 2003), so it is possible that right parietal effects may be associated with longer latencies not investigated within this study.

5.8.6, Inferior frontal phonological effects

The left inferior frontal effects associated with the phonological task condition were localised to BA45, which is consistent with reports of lesions extending into BA45 resulting in symptoms associated with Broca's aphasia (Mohr et. al. 1978). This is also consistent with evidence suggesting a link between damage to this region and phonological dyslexia (Fiez & Petersen, 1998) and with neuroimaging findings of a left inferior frontal (specifically BA44/BA45) involvement in phonological tasks (Poldrack et. al. 1999; Paulesu et. al. 1993).

Within the phonological condition, the left inferior parietal ERD reached statistical significance prior to the left inferior frontal ERD. This may have implications for the theory that inferior frontal regions close to Broca's area may represent a "subvocal rehearsal system" (Burton, 2001) whereas parietal regions (specifically BA39), may be interpreted as representing a "phonological store" (Paulesu et. al. 1993). These findings support the suggestion that access to such a parietal "phonological store" precedes the involvement of frontal phonological rehearsal systems (Burton, 2001).

Unfortunately, the temporal relationship between these regions and Wernicke's area was not within the scope of this study as group level phonological effects failed to reach statistical significance within Wernicke's region. It may be necessary to employ a different task in order to investigate the phonological effects associated with Wernicke's area. For example, it has been claimed that although Wernicke's area seems to be consistently activated by heard word repetition tasks, it is not consistently activated by reading (Price, 2000). There is also evidence to suggest that spelling to sound consistency may influence the involvement of Wernicke's area (Paulesu et. al. 2000), so the choice of stimuli used within this study may have prevented phonological effects within Wernicke's area from reaching significance at the group level.

5.8.7, Inferior frontal semantic effects

Although individual participants showed peak values of ERD within the left inferior frontal gyrus associated with the semantic task, such effects only reached statistical significance within the phonological task condition. As with inferior temporal effects, Appendix 4.5 indicates that there seems to be a relatively high level of spatial variability associated with reports of a left inferior frontal involvement in semantic processing. Based upon this, and the individual SAM images, it seems possible that such intersubject variability, possibly as a result of strategy differences, may have prevented these effects from reaching significance at the group level. It has also been suggested that the semantic demands of living/non-living decision tasks may be insufficient to produce observable left inferior frontal effects (Roskies et. al. 2001).

Despite this, the Mann Whitney representations produced for virtual electrodes placed within left inferior/middle frontal and temporal regions for four participants indicates that, in these cases, ERD within left inferior frontal regions tended to precede ERD within the temporal lobe. This is in keeping with the ERP results reported by Abdullaev & Posner (1998), and appears to support the hypothesis that left inferior frontal effects may reflect access, selection and retrieval of semantic information from "semantic stores" within the left temporal cortex (Roskies et. al. 2001, page 839), and even the suggestion that left inferior frontal regions may serve to "reactivate" semantic information that is relevant to the task (Roskies et. al. 2001). There was one exception, whereby for the virtual electrodes selected the temporal ERD peak preceded the left inferior/middle frontal peak. Out of the five left inferior/middle frontal virtual electrodes, this one was the most

superior, and was located within the left middle frontal gyrus (BA46). It is possible therefore that this ERD effect reflects a different, later process, or that strategy differences could have lead to this inconsistency.

5.8.8, Cerebellum

Within this study, right cerebellar ERD reached statistical significance at the group level within the phonological task condition. Contrary to suggestions that right cerebellar effects may be specifically linked to semantic task conditions (Roskies et. al. 2001), these findings support the hypothesis that these effects may reflect subvocal articulatory rehearsal processes, as supported by evidence from stem completion studies (Desmond et. al. 1998). The apparent discrepancy between reports of cerebellar effects specifically associated with semantic tasks and reports linking these cerebellar effects to phonological task conditions may be attributed to differences in the tasks employed in these studies. Whereas syllable counting tasks have been associated with cerebellar effects within this study, and others (Mummery et. al. 1998), Roskies et. al. (2001) reported right cerebellar effects what were specific to a synonym task when compared to a rhyme judgment task. It is possible to speculate that the rhyme judgment may have differed from the syllable counting task in a number of respects. For example, the rhyme judgment task may have been influenced by orthographic similarities between the words. Also, the time taken to complete the task may have been shorter than the time taken to complete the syllable counting task, and cerebellar effects may be dependent upon sustained subvocal articulatory rehearsal processes. It is also possible to speculate that the synonym task employed by Roskies et. al. within their semantic condition may have promoted such rehearsal processes as the stimuli were held in working memory.

The finding of statistically significant cerebellar ERD within both time windows may also be consistent with the idea that these effects represent sustained subvocal rehearsal within the syllable counting task condition (although the voxels identified within these two time windows were in different right cerebellar regions). Also both cerebellar and left inferior frontal ERD was identified within the 14-20Hz frequency band for the phonological task. Functional links have been identified between these regions (Desmond et. al. 1998; Raichle et. al. 1994) although these reports have tended to be based upon apparently semantic tasks. However, it seems possible that these tasks (which involved searching for stem completions, and generating verbs in response to nouns), also placed a

sustained demand on working memory, and therefore may have promoted subvocal articulatory rehearsal.

5.8.9, Superior / Middle frontal (BA10) effects

Both the left superior frontal (BA10) effects associated with the semantic task, and the left middle frontal (BA10) effects associated with the phonological task, were observed within the gamma frequency range (40-50Hz and 30-40Hz respectively). These effects emerged earlier within the semantic task than the phonological task, raising the possibility that delayed implicit semantic processing within the phonological task may have given rise to this effect. However, this region has been specifically linked to the process of selection from items held within working memory, for example selection between semantic attributes (Otten & Rugg, 2001; Davachi et. al. 2001). Even if implicit semantic processing occurred within the phonological condition, it seems unlikely that the syllable counting task would have lead to such semantic selection processes. The results therefore support the hypothesis that the involvement of BA10 reflects more general processes, possibly linked to selection and retrieval from working memory, that are not necessarily associated with the processing of semantic information.

By comparing the latencies at which these left frontal BA10 effects occur, a dissociation emerges between the two task conditions. Within the semantic task condition, left BA10 ERD tends to precede ERD within left temporal regions thought to represent "semantic stores", however, within the phonological task condition, significant group-level left BA10 ERD occurs after ERD within the left inferior parietal region (BA40) regarded as representing "phonological stores". This may suggest that the "reactivation" process proposed by Roskies et. al. 2001 may be specific to semantic processing, and not involved within phonological processing.

5.9, Summary

Behavioral evidence (in the form of recognition memory scores) indicated that by manipulating task demands, it is possible to vary the extent to which the semantic and phonological nature of a word is considered. By manipulating task demands in this way, the neural correlates of semantic and phonological processing were investigated using MEG. By comparing each of these conditions to a prestimulus baseline, the spatial-temporal dynamics of task related effects were identified, together with frequency effects.

Both task conditions were associated with ERD within the beta and gamma frequency ranges, with significant gamma effects confined to the left frontal gyrus (B10) in both cases. This effect occurred earlier within the semantic condition than within the phonological task condition. Within the semantic task condition, and the beta frequency band, statistically significant ERD was observed within the left middle temporal gyrus (BA39) and the right superior temporal gyrus within the 350-550ms time window, and within the left inferior parietal lobule (BA40) within the later time window of 500-700ms. This parietal effect may be the result of delayed implicit phonological processing as left inferior parietal (BA40) ERD was observed within the earlier 350-550ms time window for the phonological task condition.

Within the beta frequency band, the phonological task condition was associated with left temporal-occipital and left inferior parietal (BA40) effects within the early 350-550ms time window, and left inferior frontal ERD within the later (500-700ms) time window. Right frontal ERD also reached significance at the group level within the 350-550ms window, however, from individual SAM images it seems likely that both frontal and superior temporal ERD contributed to this effect. Cerebellar effects were significant in both time windows within the phonological task condition, supporting the notion that the cerebellum may play a role associated with sub-vocal rehearsal.

In terms of the spatial-temporal dynamics associated with the two task conditions, the main difference was in the relative timings of frontal and temporal/parietal effects. The left inferior parietal region (BA40) has tended to be linked to the notion of "phonological stores", whereas left temporal regions have been associated with "semantic stores", with left inferior frontal and left superior/middle frontal (BA10) regions being associated with executive control of processes such as selection and retrieval. Findings from this study suggest that for the semantic task, the involvement of such frontal executive systems tends to precede that of the temporal "semantic stores". However, within the phonological task condition, left inferior parietal (BA40) ERD preceded the left frontal ERD. These findings therefore indicate that there may be a dissociation between the use of such "stores" within semantic and phonological processing.

Chapter 6
Task priming.

6.1, Typical priming studies

Within the context of word processing, priming studies have tended to involve the presentation of a prime word or sound, followed by a target that is related in some way to the prime. Such behavioural studies have shown that reaction times associated with the processing of target stimuli are significantly reduced when these are preceded by semantically related word primes, (for example, within the context of a lexical decision task Rossell, Price & Nobre, 2003; Copland, Zubicaray, McMahon, Wilson, Eastburn & Chenery, 2003).

Similarly there have been reports of reduced reaction times associated with the processing of targets that are preceded by phonologically related primes. For example, Lavidor & Ellis (2003) observed a phonological priming effect associated with a lexical decision task when targets and primes were phonologically similar (homophones), while controlling for orthographic similarity.

Imaging studies have also investigated the neural correlates of these priming effects. For example, similarity of visual-perceptual semantic associations between word pairs has been found to modulate the ERP component, N400 (Kellenbach, Wijers & Mulder, 2000).

These priming studies have focused upon the priming of a certain feature of the target word, such as it's sound structure, or semantic associations. There have also been claims that operations may be primed in a similar manner (Sudevan & Taylor, 1987).

6.2, The priming of operations

Various authors claim to have shown that different "processing pathways" can be primed or prepared (the terms "priming", "task preparation", and "task-set" have been used interchangeably throughout the literature). Zevin & Balota (2000), describe an "attentional control" hypothesis whereby participants can bias their processing style in order to focus on either a sublexical route (whereby pronunciations are produced based on spelling-to-sound mappings), or a lexical route (whereby the whole word is mapped onto a lexical

representation which has the appropriate pronunciation stored with it). Nonwords have been used to prime a sublexical route, as they have no lexical representation their pronunciation apparently requires the use of spelling-to-sound conversion rules. Conversely, there are words that cannot be pronounced using spelling-to-sound conversion rules, (for example, exception words such as "choir"). These have therefore been used to prime the use of a lexical route.

Various studies have investigated the "attentional control hypothesis" using list composition manipulations. For example, Simpson & Kang (1994) asked participants to read Korean Hangual words of different frequencies within lists which, in certain conditions, also contained nonwords and Hanza script (which contains little information regarding phonology). Reaction time data suggested that the inclusion of nonwords eliminated a frequency effect in the Hangual words. This can be interpreted as indicating that the inclusion of nonwords biased participants to depend upon a sublexical route to reading, which was not susceptible to frequency effects. In support of this interpretation, the inclusion of Hanza script (believed to prime a lexical-semantic route), resulted in a fairly large frequency effect

Other such list manipulation studies have produced similar findings, for example, Tabossi & Laghi (1992) reported that semantic priming effects between Italian words were diminished within lists that included nonwords, and Content & Peereman (1992) found that introducing nonwords increased the size of a regularity effect whereby regular French words were processed faster than irregular French words. However, modulation of a regularity effect was not observed within a similar experiment using English stimuli (Coltheart & Rastle, 1994). Zevin and Balota (2000) therefore derived a more powerful paradigm in order to investigate this using English.

Within a set of four experiments, participants were asked to name five primes, followed by a target. Targets and primes were either nonwords, or low frequency exception words. The naming of nonwords was believed to prime a dependence upon the sub-lexical route for reading, whereas the naming of low-frequency exception words was believed to prime a reliance upon the lexical route. Unlike the list manipulation studies, this paradigm was believed to be more powerful as it ensured that each target was preceded by five primes of the appropriate type.

Results obtained from these studies show that the reaction time associated with the naming of nonword targets was significantly reduced when they were preceded by nonword primes, compared to the condition involving low-frequency exception word primes. The authors interpret this as suggesting that unlike the low-frequency exception words, the nonwords primed a sub-lexical route to reading, which lead to a behavioural advantage in the naming of nonword targets.

Results regarding the number of regularisation errors made within each condition are also in keeping with this interpretation. Regularisation errors are made when sublexical spelling-to-sound conversion rules are used to pronounce an exception word. The authors report a significant increase in the number of regularisation errors following nonword primes rather than low-frequency exception word primes. Again this is consistent with the suggestion that nonwords can prime a sub-lexical route to reading.

Although consistent with an "attentional control hypothesis", the authors acknowledge that both of these results may be attributed to an "expectancy effect" for a certain type of stimulus (e.g. a word or a nonword). This issue was addressed in another experiment in which the targets consisted of low frequency exception words and low-frequency regular words. A regularity effect was observed whereby low-frequency regular word targets were named faster than low-frequency exception word targets. Reaction time results show that this effect was larger in the condition in which the targets were preceded by nonword primes, and again there were more regularisation errors associated with this condition. Both of these results suggest that attention had been biased towards a sub-lexical route, inhibiting the lexical-route required for low-frequency exception word reading.

Although these data seem to be consistent with those obtained from list composition studies, Kinoshita & Lupker (2003) failed to replicate either the difference in the number of regularisation errors, or the difference in the regularity effect between the two prime conditions, as reported by Zevin & Balota (2000). The studies were not exactly the same as the stimuli differed in terms of the number of letters and the number of syllables. Kinoshita & Lupker (2003) also used fewer primes for each target. Despite these differences, the authors conclude that rather than supporting an "attentional control" mechanism, their results support a "time-criterion account", which has also been described as the "deadlines hypothesis" (Zevin & Balota, 2000). According to this approach participants adjust a timing criterion for the initiation of responses based upon their response latency for the previous trial (in this case the naming of the prime words).

Kinoshita & Lupker (2003) suggest that readers do not always initiate articulation as soon as they are able, and that the inclusion of nonwords, which can be read quickly, sets the time-criterion to a lower level. They argue that this time-criterion account can explain the results of the list composition studies, and also those produced by Zevin & Balota (2000), except for the modulation of the regularity effect, and the differences in the number of regularisation errors, both of which Kinoshita & Lupker (2003) failed to replicate.

6.3, Priming using instructions (task cues)

One way to investigate possible priming effects associated with different processing routes, without introducing confounds associated with the use of words and nonwords as primes, is to use task instructions, or "task cues". These task cues can be presented in advance of a stimulus in order to inform the participant which task to perform. In this way the same stimuli can be used within each condition, with just the task-cue changing. However, this paradigm also has methodological problems associated with it, and the task cues are also susceptible to confounds, for example, in terms of the association strength between the cue and the relevant task set (Arbuthnott & Woodward, 2002).

Brass & Cramon (2002) employed this paradigm. Participants were presented with numbers with which to perform one of two tasks. "Task cues" took the form of geometric shapes. When the task cue was a square, this indicated that participants should determine whether the number was smaller or greater than 30, whereas the presentation of a diamond shape indicated that they should determine whether the number was odd or even. In one of the conditions the task cue appeared in advance of the number (the target), and in another both the cue and the target appeared simultaneously. Reaction time results showed a significant main effect of cueing whereby the presentation of a task cue in advance of the target stimulus was associated with significantly reduced reaction times, compared to the condition in which both appeared simultaneously.

This methodology suffers from two main disadvantages (Rogers & Monsell, 1995). Unlike the condition in which the task cue precedes the target stimulus, within the condition involving simultaneous presentation of the task cue and the target, performance is likely to be influenced not only by the lack of opportunity to prepare the task, but also by the time taken to process the task cue. It has been suggested that such "perceptual

interference" may account for the apparent behavioural advantage associated with priming a task in advance of the stimulus (Meiran, 1996). Another disadvantage of using such a paradigm is that it is difficult to control for which task the participant may have anticipated in the absence of a valid precue.

A paradigm that may partially overcome these difficulties is one in which the interval between the cue and the stimulus is varied in order to vary the time available for task preparation. Such a paradigm has produced results that show performance to improve with increasing time between the cue and the target (Sudevan & Taylor, 1987). Although one explanation for this is that the behavioural advantage is brought about by the longer period of time available for task preparation, it is also possible that, although the cue and the target are not presented simultaneously, presenting them with a short inter-stimulus-interval leads to an interference effect associated with perceptual encoding (Meiran, 1996).

It has been argued that this interpretation could also account for the results of studies (for example, Biederman, 1973) reporting a similar behavioural advantage when the target stimulus precedes the instructional cue (Meiran, 1996). Another possible interpretation, which would also account for the similarity between the results from the cue-target condition and the target-cue condition, is that the cue is used in order to predict target onset, rather than to perform a task-specific preparation process (Meiran, 1996). In support of this possibility, it has been argued that when the amount of time available for task preparation is randomly varied, the effect on reaction time is mediated by the prediction of target onset (Niemi & Näätänen, 1981).

6.4, Task-switching

One paradigm that does not involve the simultaneous presentation of a task cue and a target stimulus, nor the manipulation of the inter-stimulus-interval between the two, is that employed within standard "task switching" experiments. Within these paradigms participants switch between two or more tasks during one block of trials. Task cues precede each stimulus and inform the participant which task to carry out. Trials in which the participant has had to switch task have been consistently associated with significantly longer reaction times ("switch cost") compared to those that do not involve a task switch (Rogers & Monsell, 1995; Brass & Cramon, 2002; Mayr & Kliegl, 2003; Meiran, 1996).

A number of authors have explained such "switch cost" effects in terms of persisting activation or suppression of "task sets" (Koch, 2001; Arbuthnott & Woodward, 2002). A task set has been defined as "an effective intention to perform a particular task, regardless of which of the range of task-relevant stimuli will occur" and described as an important component of executive control (Rogers & Monsell, 1995, page 207). Many authors account for the switch cost in terms of a process of task-set reconfiguration (Koch, 2001; Meiran, 1996).

Experimental results also support the idea of the switch cost being partially attributable to a task-set reconfiguration process occurring at the point at which the task cue is presented. For example, Mayr & Kliegl (2003) conducted two comparisons with which they claim to have separated a component associated with the cue-switch and a component associated with the task-switch. Firstly they compared trials in which neither the task-cue nor the task changed with trials in which the cues changed, but the task remained constant. This contrast was designed to isolate the effects of changing only the task-cue. In order to isolate the effects of task switching that were confined to the target processing stage, trials in which the cue changed but the task stayed constant were compared to trials in which both the cues and tasks changed. Results suggest that most of the total switch cost is not due to a change in task per se, but due to a changes in cue-associated processes, in support of the task-set reconfiguration approach.

Also in keeping with this idea are the findings that switch costs are reduced with increasing cue-target interval duration (Meiran, 1996; Mayr & Kliegl, 2003), suggesting that the cue-target interval might be being used for the time-consuming process of task-set reconfiguration. Mayr & Kliegl (2003) produced results which indicate that the variation in cue-target interval only affects the cue-switch component and not the task-switch component. This further supports the notion that it is a time-consuming reconfiguration of the task-set, in response to the presentation of a task cue, that contributes to the switch-cost effect.

6.5, Task sets

The process of priming a task set, or "cognitive strategy" (Meiran, 1996), has been defined only in abstract terms. Authors have described the process as reflecting "endogenous task-management processes" (Brass & Cramon, 2002, page 1047), and "endogenous control processes" (Arbuthnott & Woodward, 2002, page 19). Others have

focussed upon the process of retrieving task-rules from long-term memory, which may be justified by results indicating that switch costs may increase as a function of the long-term-memory demand of the switched-to task (Mayr & Kliegl, 2000). Another approach has been to view this process in terms of "executive aspects of attention that aid in the selection of task-relevant information" Banich, Milham, Atchley, Cohen, Webb, Wszalek, Kramer, Liang, Barad, Gullett, Shah & Brown, 2000).

6.6, The neural correlates of task set manipulations

There have been various ways in which the neural correlates of task-set priming have been investigated. For example, it has been argued that the task-switching paradigm is one of the best means by which to study executive control (Meiran, 1996). In keeping with the findings of patients with frontal lobe lesions showing impairment in their ability to shift between tasks (Shallice & Burgess, 1991), the process of task-shifting has been linked to inferior frontal differential effects using MEG (Periáñez, Maestú, Barceló, Fernández, Amo & Alonso, 2004), PET (Konishi, Nakajima, Uchida, Kameyama, Nakahara, Sekihara & Miyashita, 1998), and prefrontal effects using fMRI, (Sohn, Ursu, Anderson, Stenger & Carter, 2000; Dove, Pollamann, Schubert, Wiggins, & Cramon, 2000). These studies have also identified various other regions as showing an involvement in the processes of task-switching, such as the anterior cingulate cortex (BA 24 and 23) and the supramarginal gyrus (BA40) (Periáñez et. al. 2004).

Similar prefrontal regions (BA44 and 46) have been identified as playing a substantial role in "imposing an attentional set" during a variation of the Stroop experiment in which participants are required to focus their attention upon task-appropriate aspects of the stimuli (Banich, Milham, Atchley, Cohen, Webb, Wszalek, Kramer, Liang, Barad, Gullett, Shah & Brown, 2000). Weissman, Mangun & Woldorff (2002) describe a frontoparietal network associated with the process of selective attention, whereby prefrontal regions play a role in maintaining task goals, and parietal regions "focus attention on task-relevant features" (page 1266).

Each of these studies have investigated the neural correlates associated with various task-set manipulations, rather than those directly associated with the process of task preparation. Brass & Cramon (2002) directly measured the neural correlates associated with the presentation of a task cue during trials in which the cue was shown, but not the target. Results indicate that the presentation of a task cue was associated with activity

within a frontal network, including the junction of the precentral sulcus and the inferior frontal sulcus in both hemispheres, and bilateral middle frontal regions. The activated network is described as being similar to those identified by studies designed to investigate task-switching effects (Brass & Cramon, 2002). The authors conclude that the inferior frontal junction "is responsible for implementing a task set, which requires the selection of relevant stimulus-response mappings for the upcoming task" (Brass & Cramon, 2002, page 914).

There are, however, a number of potential drawbacks associated with the use of such a paradigm. Firstly, task cues are not always followed by targets, so it is possible that participants may not have prepared for a task to the same extent as they would have done had they known that they would definitely be conducting the task. It could also be argued that cue-only trials may have involved additional cognitive processes caused by the non-appearance of a target. In the case of the study reported by Brass & Cramon (2002), the authors argue against this explanation by pointing to the fact that the same frontal regions were also involved with the trials that involved both a cue and a target, however it seems that the precise role played by these regions in task preparation is poorly understood.

Another drawback associated with this study is that it investigated the process of task preparation without differentiating between the different tasks that are being prepared. Based upon the definition of a task set as a "neurocognitive state in which an up coming task is prospectively configured" (Sakai & Passingham, 2003), it seems reasonable to assume that this task set should be specific to the task that is due to be performed. In support of this, differential effects have been identified between the preperation of different tasks. For example, an ERP study reported task-specific slow electric potentials within the time interval between cue presentation and target presentation, when cues primed participants to either compare pairs of faces, or pairs of dot patterns which were superimposed onto the face pictures (Tarkka & Mnatsakanian, 2003).

Sakai & Passingham (2003) investigated the neural correlates of different task sets using fMRI. Participants were required to remember either a sequence of letters, or the sequence of spatial positions in which the letters were presented. In one task condition participants were instructed to recall the items in the order in which they had been presented (the forward-task), and in another to recall the items in the reverse order (the backward-task). Task-cues informed participants of both the domain to focus on (verbal or spatial) and the operation they would perform (i.e. the order in which the items should be

recalled). It was assumed that the presentation of these cues would lead to the preparation of task-sets, so their neural correlates could be investigated.

As a result of comparisons between the different task conditions, the authors identified three different effects. Firstly, by comparing trials associated with the presentation of cues priming a verbal task to those priming a spatial task, "domain specific activations" were identified. Activation in the posterior portion of the superior frontal sulcus (BA8) and the superior parietal lobule was significantly higher before the spatial task than before the verbal task. In contrast, activation in the posterior part of the left inferior frontal gyrus (BA44, Broca's area), the posterior part of the left superior temporal gyrus (BA22, Wernicke's area), inferior temporal and middle temporal regions, was significantly higher before the verbal tasks than before the spatial tasks.

Sustained activation within the anterior prefrontal cortex (BA10) was observed in response to the task cue, regardless of the domain, and the order in which the items should be recalled. The location of this activation was consistent between each of the task conditions, it was time-locked to the presentation of the instruction, and the activation was significantly stronger during the instruction delay than during the pre-instruction period. These results are in keeping with previous claims of rostral prefrontal cortical regions showing an involvement in "prospective memory" studies which require participants to maintain delayed "intentions to act" regardless of the task (Burgess, Scott & Frith, 2003). They are also consistent with claims that these regions are associated with a "retrieval mode" (Lepage, Ghaffar, Nyberg & Tulving, 2000), and may therefore play a general role in the retrieval of task rules.

Sakai and Passingham (2003) extend these findings by reporting results which suggest that the anterior prefrontal cortex interacts with posterior prefrontal areas in different ways according to the specific task to be performed. Although the magnitude of activation did not show operation-specificity, inter-regional interactions during the instruction delay did differentiate between the operations that were being primed. The authors report a significant correlation between the anterior prefrontal activation and the superior frontal activation only in response to the "verbal-backwards" task cues. The correlation between the anterior prefrontal activation, and the inferior frontal activation was significantly higher in response to the "verbal-backwards" task cue, compared to the other conditions.

The results reported by Sakai & Passingham (2003) highlight the importance of differentiating between different tasks when investigating the neural correlates of task priming. Besides being specific to a task, it seems reasonable to assume that there will be similarities between the process of establishing a particular task set, and the process of performing that task on a given stimulus. Sakai & Passingham (2003) report that areas that showed pre-task activity were also active during task performance, although the task-specificity of these effects is unclear.

Chapter 7

Study 2: Semantic and phonological task set priming and stimulus processing investigated using Magnetoencephalography.

7.1, Abstract

Within the study reported in Chapter 5, task-dependent differential effects were observed which apparently provide information regarding the neural substrates of the use of semantic and phonological "processing pathways". Behavioural evidence using word and nonwords as primes suggests that these two processing pathways may be selectively primed or inhibited (Zevin & Balota, 2000), although these studies may also be susceptible to confounds associated with the choice of primes.

The MEG study reported within this chapter represents an attempt to extend the investigation in a number of ways. The aim was to investigate the priming of lexical and sublexical routes to reading, as described by Zevin & Balota (2000). However, unlike the study conducted by Zevin & Balota (2000), the two types of processing were primed using single word task instructions which were presented prior to stimulus onset, rather than nonwords and low-frequency-exception words (which were believed to bias the sublexical and the lexical routes respectively). This has a number of advantages. Firstly, it removes confounds associated with the use of words and nonwords as primes, such as speed of reading (believed to be influential according to the "time-criterion account" described by Kinoshita & Lupker (2003)). It also removes confounds associated with the choice of primes, for example, different prime words may vary in terms of their strength of association with the target stimulus. It also removes confounds associated with various task demands, such as response planning.

The use of MEG in the investigation of task priming also provided a number of advantages over other imaging methods. The enhanced temporal resolution offered by MEG allowed investigation of the evolution of the task-priming process, with millisecond resolution. This was also advantageous in terms of the paradigm, as it meant that relatively short inter-stimulus intervals between the task cue and the target could be used without the need to incorporate trials in which a task-cue was presented, but not followed by the presentation of a target stimulus (as in the case of the fMRI study reported by Brass & Cramon (2002)). This avoids problems that may be associated with participants failing to

establish a sufficient level of expectation that a target will follow, or with target stimuli unexpectedly failing to appear.

As discussed in Chapter 6, the results reported by Sakai & Passingham (2003) highlight the importance of differentiating between different tasks when investigating the neural correlates of establishing a task set. By analysing the MEG data associated with the presentation of these task primes, differential effects associated with semantic and phonological task priming were identified. The study reported within this chapter aimed to extend the approach by directly comparing task-specific effects associated with the presentation of the task cue, and those associated with the presentation of the target stimulus. In this way the neural correlates associated with establishing a particular task-set and with conducting that task, could be compared, and any similarity between the task-specificity of these two processes identified.

Two main effects were observed. Firstly, statistically significant ($p<0.05$) ERD was observed within left superior frontal, and left middle temporal regions in the semantic task condition and within both the epoch associated with the presentation of the task prime and the epoch associated with the presentation of the target stimulus. Conversely, within the phonological task condition, late superior frontal, parietal and cerebellar ERD was identified within both task prime and target epochs.

In this way significant differential effects were observed in response to the priming of semantic and phonological tasks, i.e. preceding specific semantic/phonological processing requirements. Furthermore, a number of parallels were identified between the task related differential effects associated with the presentation of the task prime and presentation of the target word. This extends the work on the priming of semantic and phonological tasks. It also extends the findings relating to task dependent differential effects observed in response to a task cue, as it considers these effects alongside those associated with task-specific stimulus processing, and identifies a number of parallels between the two.

At certain voxels within the left middle temporal gyrus and left inferior frontal gyrus the onset of the semantic task prime was associated with statistically significant ($p<0.05$) ERD, whereas onset of the phonological task prime task was associated with ERS. Such a dissociation was also observed between the two epoch types. Whereas voxels within the right superior temporal gyrus and the left middle temporal gyrus were associated

with significant ERS within the phonological task prime condition, they were associated with significant ERD within the semantic target epoch. Various interpretations for this ERD/ERS dissociation are discussed.

In terms of language processing, it maybe that the process of task-priming, as facilitated by paradigms such as this, could enable the investigation of different processing frameworks (in this case semantic or phonological processing) without the potential drawbacks associated with relying upon data obtained during the processing of different target stimuli, such as the introduction of confounds associated with the choice of target stimuli.

7.2, Method

The participants and stimuli were exactly the same as those described within the Chapter 5. The same datasets were used within the two studies, but in the case of this study data analysis was performed on epochs corresponding to the onset of the task prime, rather than the target stimulus.

7.2 1, MEG recording and coregistration with MRI data

MEG data was collected using a 151-channel CTF Omega system (CTF Systems Inc., Port Coquitlam, Canada). The data was collected at a sampling rate of 625Hz. Following data acquisition the shape of the participants head was digitised using a 3-D digitiser (Polhemus Isotrack). This surface was matched to that extracted from the participant's anatomical MRI, using Align (www.ece.drexel.edu/ICVC/Align/align11.html) so that the MEG data obtained from each participant was coregistered with their anatomical MRI scan.

7.2.2, Data Analysis

Epochs containing eye blink artefacts were identified by visual inspection, and omitted from further analysis. As the literature (mainly consisting of fMRI and PET studies) failed to provide consistent reports of time windows of interest for task priming effects, SAM analysis was performed using overlapping 200ms time windows in order to span the 800ms following onset of the task prime (i.e. 0-200ms, 100-300ms, 200-400ms, 300-500ms, 400-600ms, 500-700ms and 600-800ms). Using these time windows, comparisons were made between the semantic and phonological conditions, and between each type of task prime and a pre-stimulus 200ms baseline (which, as in the previous study, occurred prior to the onset of the task prime). For each of these comparisons, and for each participant, a 3D statistical parametric map was produced for each of the frequency bands (8-13Hz, 14-20Hz, 20-30Hz, 30-40Hz and 40-50Hz). These images were averaged using Group SAM and the statistical significance of differential effects assessed using SnPM (as described in Chapter 2).

7.3, Results

7.3.1, Differential effects

As a result of Group SAM and SnPM analysis, regions were identified in which significant effects were observed (Table 7.1). Unlike the analysis associated with the target epoch, three regions were identified in which significant semantic/phonological differential effects were observed ($p<0.05$) within the task prime epoch. The first effect was identified in the 0-200ms time window within the left medial/inferior frontal gyrus (BA10/11), the second in left middle temporal gyrus between 200ms and 400ms, and the third within the 400 to 600ms time window, in the right inferior temporal gyrus (figure 7.1).

Each of these differential effects are considered, together with the results of the comparisons between each of the task prime conditions and a prestimulus baseline. Results from the epoch associated with the presentation of the target word are presented when parallels can be observed between these results and those obtained for the epoch associated with the presentation of the task prime.

7.3.2, Inferior Frontal effects

Group SAM analysis revealed that the voxel identified from the semantic v phonological SnPM analysis was associated with a power increase (indicative of ERS), within the 30-40Hz frequency band, in the phonological task prime condition ($T=2.56$), but not in the semantic task prime condition ($T=-0.06$).

For each participant a virtual electrode was placed within the voxel corresponding to the one on the template brain in which statistically significant group level semantic/ phonological differential effects were observed. Mann Whitney representations were produced from the virtual electrode output, and frequencies identified at which peak values of the Mann Whitney Z statistic could be observed within the first second after prime onset and within the first second of target onset.

Eight out of the ten participants showed significant ($Z>2$) semantic/phonological differential effects within both the target and prime epochs. In each of these cases the semantic task was associated with ERD and the phonological task associated with ERS (an example is shown in figure 7.2). Although there was a certain degree of individual variability regarding the frequency band in which these effects were observed, all of these effects occurred between 20-50Hz.

Table 7.1, The co-ordinates of the voxels showing significant effects ($p<0.05$) within the epoch associated with the presentation of the task cue, for the two task conditions relative to the prestimulus baseline, identified using Statistical NonParametric Mapping. Italics denote the effects associated with ERS within the stimulus condition compared to the prestimulus baseline, the others relate to ERD within the stimulus condition.

PRIME	**Semantic v Baseline**	**Phonological v Baseline**	**Semantic v Phonological**
0-200ms			
8-13 Hz	-	-	-
14-20 Hz	-	-	-
20-30 Hz	-	-	-
30-40 Hz	-	-	Next to left medial frontal gyrus/inferior frontal gyrus near BA10/11 -54, 51, -15
40-50 Hz	-	-	-
100-300ms			
8-13 Hz	-	-	-
14-20 Hz	-	*Left temporal lobe next to left middle temporal gyrus -48, -36, -6*	-
20-30 Hz	Left occipital lobe cuneus BA19 -21, -90, 27	Left middle occipital gyrus -24, -93, -3	-
30-40 Hz	-	-	-
40-50 Hz	-	*Right superior temporal gyrus 54, -36, 6*	-

200-400ms			
8-13 Hz	-	-	-
14-20 Hz	-	-	-
20-30 Hz	Next to left superior frontal gyrus BA9, -9, 63, 51	Left middle occipital gyrus -24, -93, -3	Left middle temporal gyrus -51, -42, 0
30-40 Hz	-	-	-
40-50 Hz	Left superior frontal gyrus Left superior frontal gyrus BA6 -24, 12, 78 and –21, 6, 72		
300-500ms			
8-13 Hz	-	-	-
14-20 Hz	-	-	-
20-30 Hz	-	Next to left cerebellum -60, -69, -27	-
30-40 Hz	-	Left superior parietal lobule next to BA7 (includes precuneus) -24, -66, 60 and -21, -66, 48	-
40-50 Hz	-	-	-
400-600ms			
8-13 Hz	-	-	-
14-20 Hz	-	Right middle occipital gyrus	-

		39, -72, 6	
20-30 Hz	-	-	Next to right inferior temporal gyrus 48, -3, -51
30-40 Hz	-	Next to left middle frontal / superior frontal gyrus BA9 (near BA10) -36, 51, 42	-
40-50 Hz	-	-	-
500-700ms			
8-13 Hz	-	-	-
14-20 Hz	-	-	-
20-30 Hz	-	-	-
30-40 Hz	-	-	-
40-50 Hz	-	-	-
600-800ms			
8-13 Hz	-	-	-
14-20 Hz	*Right middle occipital gyrus* *33, -81, 9*	-	-
20-30 Hz	-	-	-
30-40 Hz	-	-	-
40-50 Hz	-	Right parietal precuneus 6, -69, 39	-

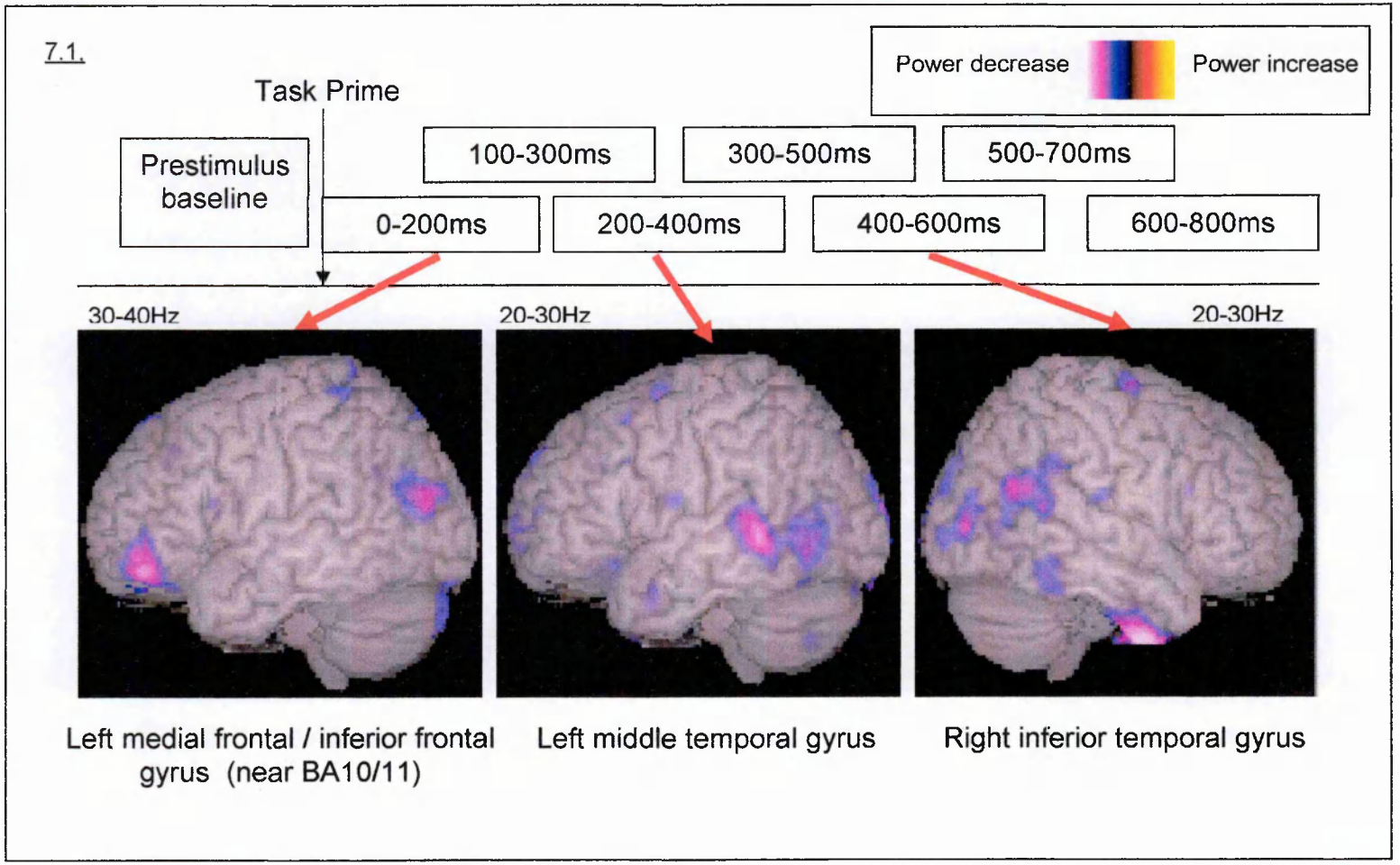


Figure 7.1, SnPM results showing the timing, frequency range and location of group level differential effects between the two task prime conditions. Within each of these regions a voxel was identified at which statistically significant ($p<0.05$) differential effects were observed (talairach co-ordinates: –54,51,-15; -51,-42,0, and 48,-3,-51). The images show values corresponding to $-3>t>3$.

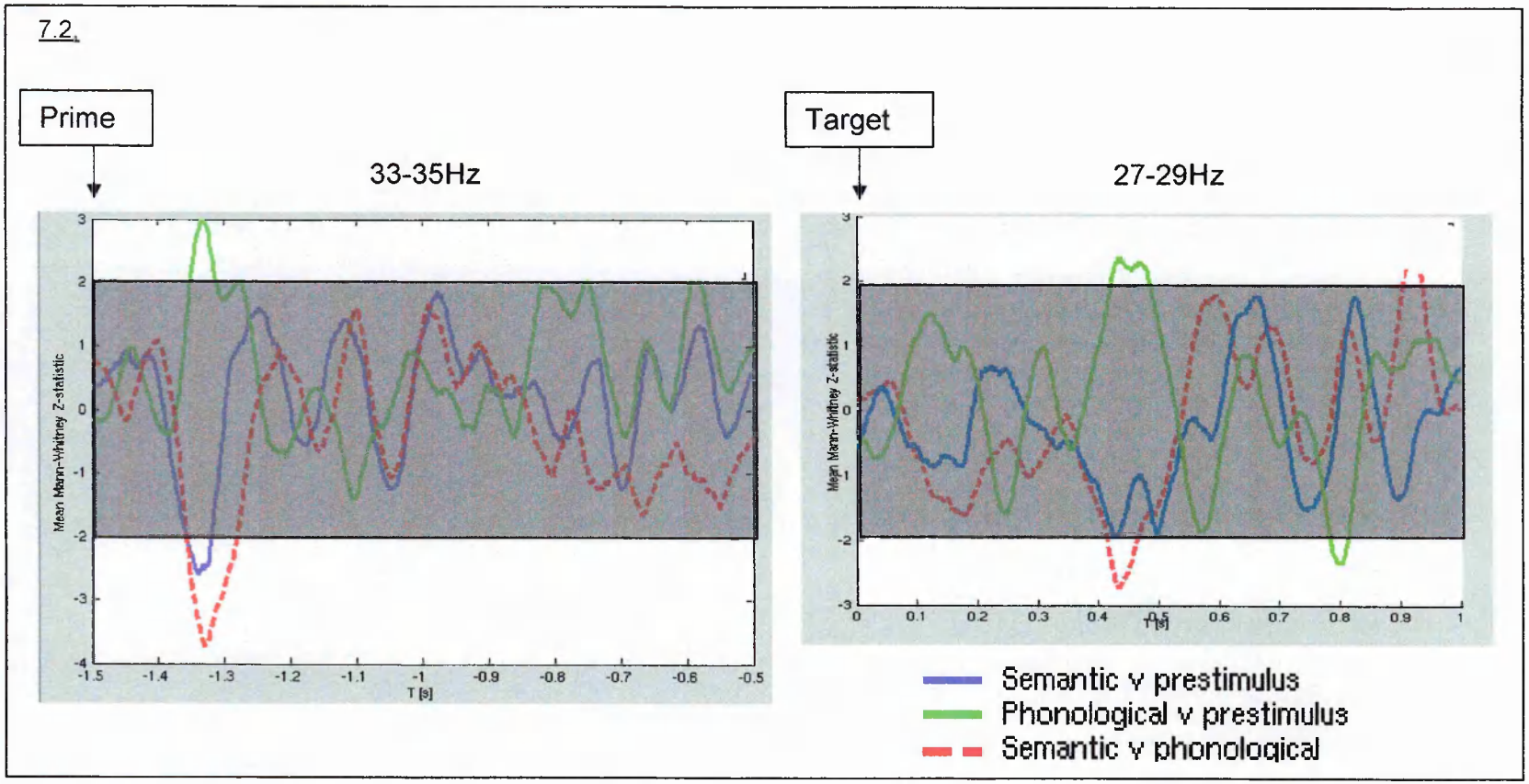


Figure 7.2. The Mann Whitney Z statistic as a function of time for differential effects between the semantic and the phonological task conditions, the semantic v prestimulus baseline comparison, and the phonological v prestimulus baseline comparison for a virtual electrode placed within the left inferior frontal gyrus (BA10) of one participant, for both the task prime and target epochs. 2Hz wide frequency bands are shown (33-35Hz for the task prime epoch, and 27-29Hz for the target epoch). This shows that in both task prime and target epochs significant (Z>2) differential effects were observed which were associated with ERS within the phonological task condition, and ERD within the semantic task condition.

7.3.3, Left Middle Temporal effects

The Group SAM rfx images for the 200-400ms, 20-30Hz task prime v baseline comparisons indicate that the statistically significant ($p<0.05$) differential effect observed within the left middle temporal gyrus was associated with ERD for the semantic task prime condition. The voxel in which significant differential effects emerged (figure 7.3) was associated with a t value of –2.05 for the semantic v baseline comparison, and $t = -0.22$ for the phonological v baseline comparison.

In the previous time window (100-300ms), the phonological task prime condition had been associated with statistically significant ERS within a left middle temporal voxel (figure 7.3). This effect was observed within the 14-20Hz frequency band. The two voxels are within close proximity (approximately 9mm apart).

The semantic v prestimulus comparions for the target epoch also revealed significant ERD at the border between the left middle temporal gyrus (within the 350-550ms time window, and the 20-30Hz frequency band), and the occipital lobe. The voxel in which this effect reached significance is more posterior to those showing significant effects associated with the presentation of the task prime (figure 7.3). The voxel is approximately 39mm away from the left middle temporal voxel in which the significant differential effect had been observed in response to presentation of the task prime.

7.3.4, Right Inferior Temporal effects

The right inferior temporal voxel (figure 7.4) identified as showing a statistically significant differential effect between the semantic and phonological task prime epochs (400-600ms, 20-30Hz) was associated with ERS within the phonological task prime condition ($T=2.56$), but not within the semantic task prime condition ($T=-1.28$). Differential (semantic v phonological) task effects associated with the presentation of the target did not reach statistical significance at the group level within this, or any other, area.

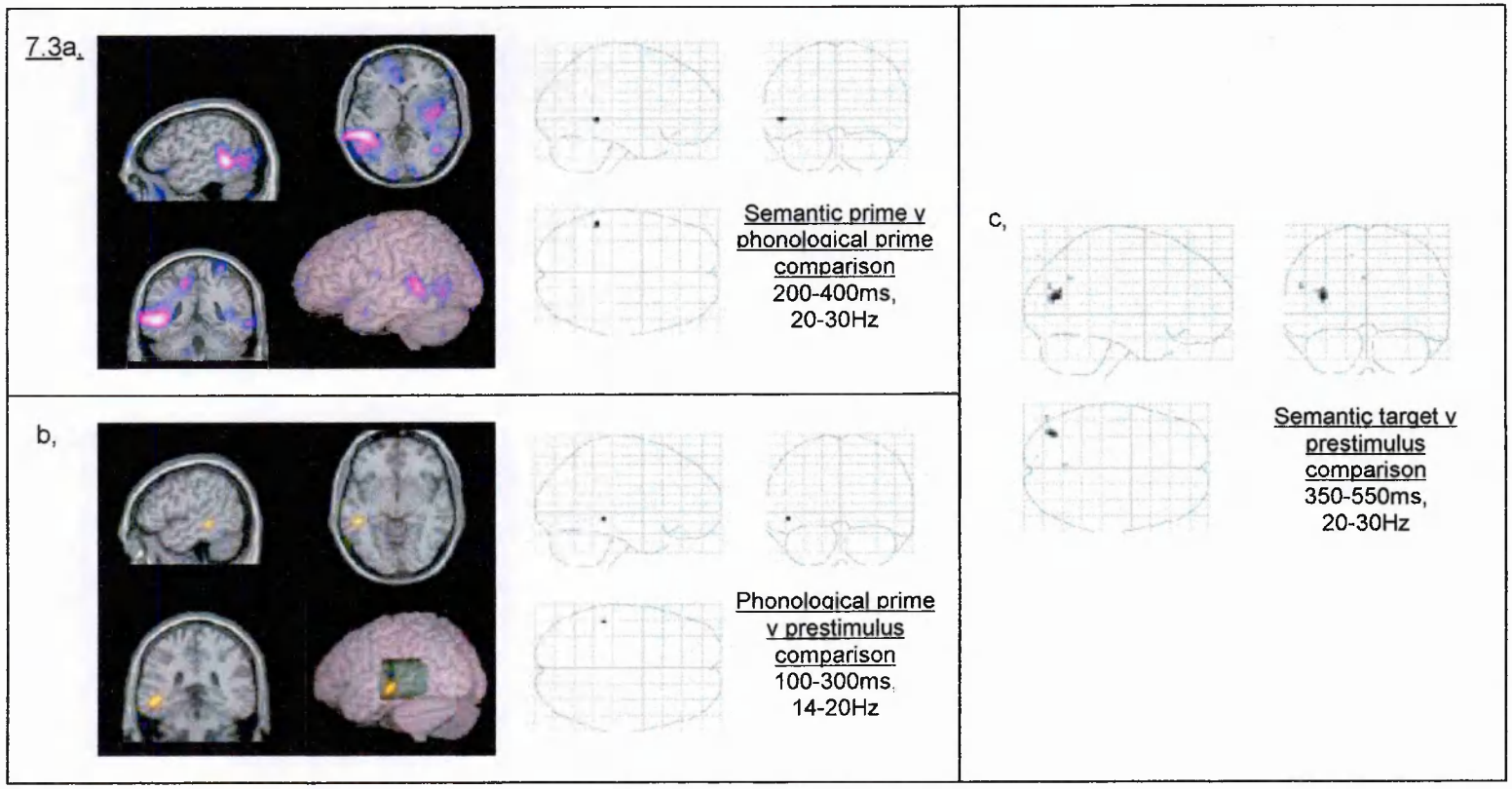


Figure 7.3, SnPM results showing statistically significant ($p<0.05$)

a) differential effects between semantic and phonological task primes within 200-400ms, and 20-30Hz (which arose from strong ERD associated with the semantic task prime condition) (the voxel in which significant effects were observed corresponds to talairach co-ordinates –51, -42, 0),

b) ERS within the phonological task prime condition within 100-300ms, and 14-20Hz, (the voxel in which significant effects were observed corresponds to talairach co-ordinates –48, -36, -6), and

c) ERD within the semantic task condition for the target epoch, identified within 350-550ms, and 20-30Hz (the voxels in which significant effects were observed correspond to talairach co-ordinates –36, -75, 15 and -54, -78, 24). The images show values corresponding to –3>t>3.

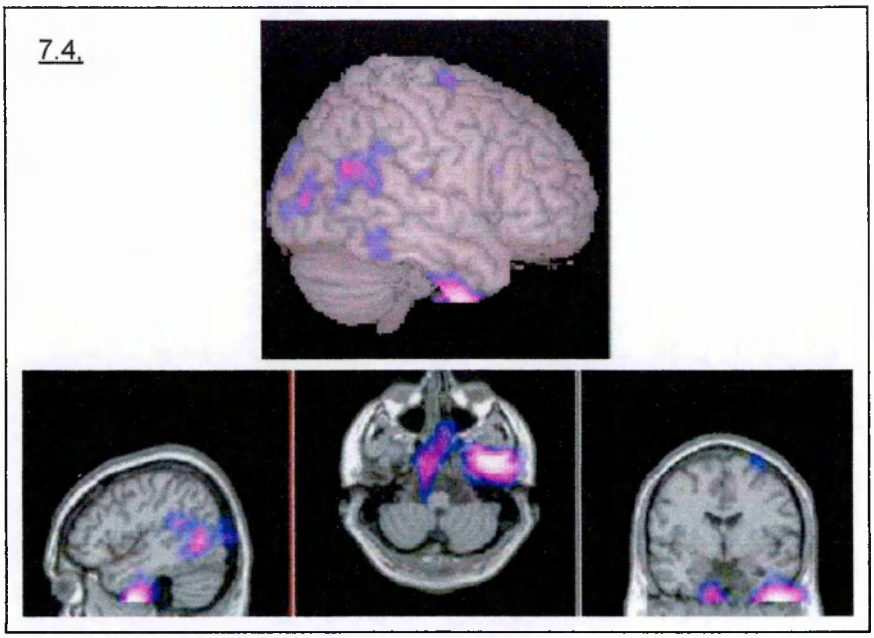


Figure 7.4. SnPM results for the semantic v phonological task prime comparison. Statistically significant differential effects ($p<0.05$) were observed within a right inferior temporal voxel (talairach co-ordinates 48, -3, -51) (400-600ms, 20-30Hz), and this was associated with ERS in the phonological task condition. The images show values corresponding to $-3>t>3$.

7.3.5. Right Superior Temporal effects

The phonological task prime condition was associated with superior temporal ERS. This ERS reached statistical significance at a voxel within the superior temporal gyrus for the 100 to 300ms, 40 to 50Hz phonological task prime v prestimulus comparison. This voxel is within close proximity of a right superior temporal voxel in which statistically significant ($p<0.05$) ERD associated with the semantic target condition between 350 and 550ms and 14 to 20Hz (figure 7.5). The two voxels are approximately 26mm apart.

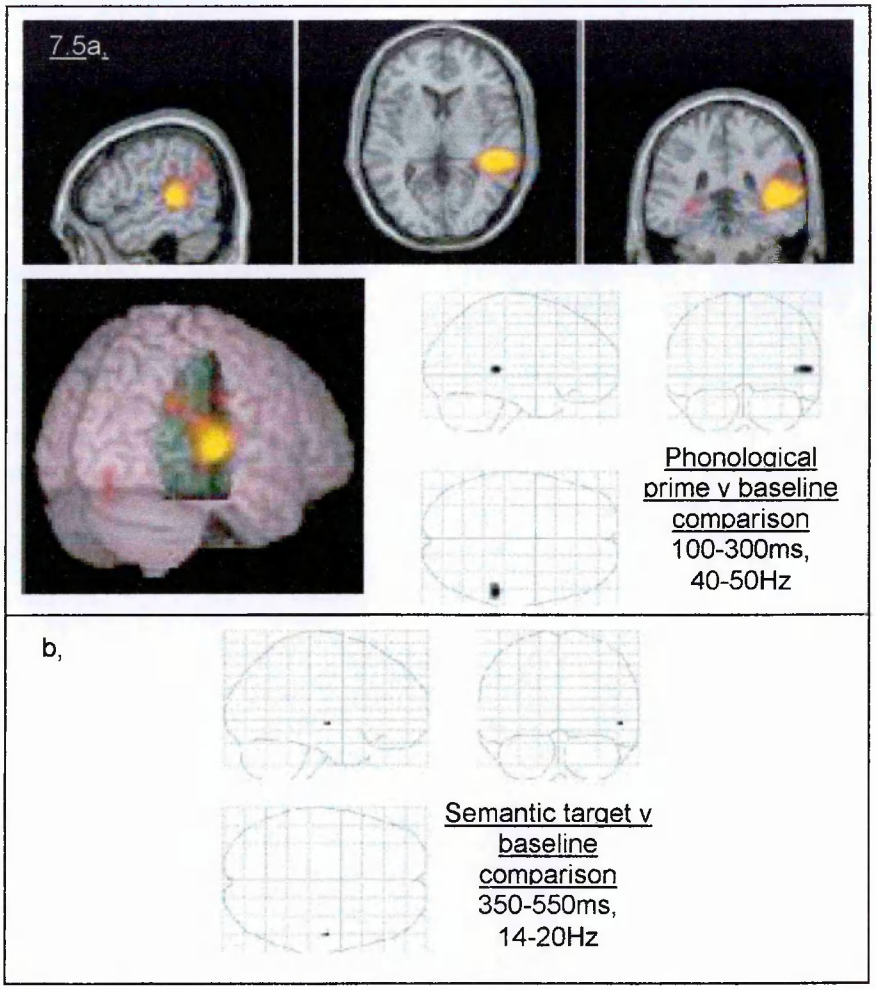


Figure 7.5. Group SAM and SnPM results showing

a) statistically significant right superior temporal ERS associated with the phonological task prime condition, within the phonological v prestimulus comparison (within the 100-300ms time window, and the 40-50Hz frequency band, talairach co-ordinates 54, -36, 6) and

b) statistically significant right superior temporal ERD associated with the semantic target condition, within 350-550ms, and 14-20Hz (talairach co-ordinates 51, -12, -3). The images show values corresponding to $-3>t>3$.

7.3.6. Left Middle Frontal / Superior Frontal Effects

Another statistically significant frontal effect was ERD observed within the left superior frontal gyrus for the semantic task prime condition compared to the prestimulus baseline ($p<0.05$). This effect was associated with the 200-400ms time window and the 20-30Hz frequency band.

This voxel is in close proximity to a voxel identified as showing significant ERD associated with the target presentation also within an early time window in the semantic task condition (figure 7.6). The two voxels are approximately 20mm apart.

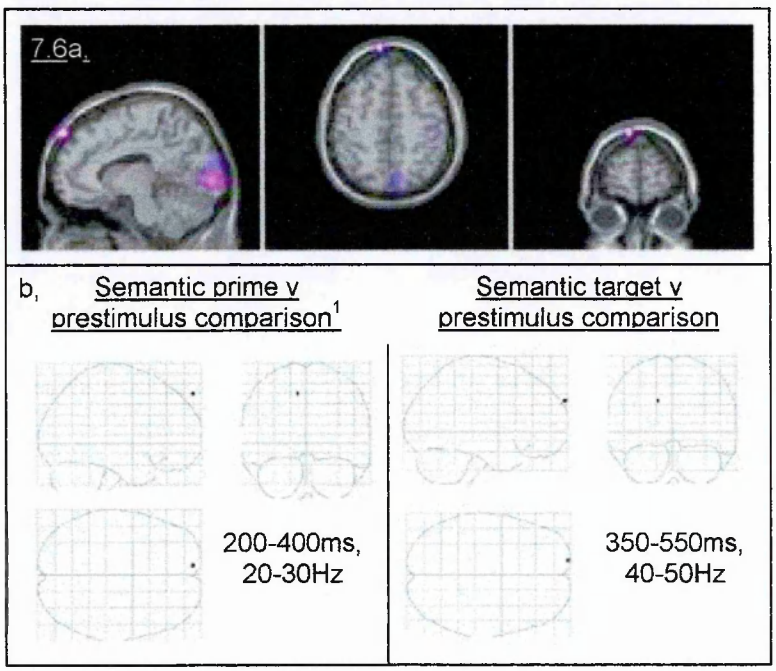


Figure 7.6. a) SnPM results showing statistically significant ($p<0.05$) superior frontal ERD associated with the semantic task prime, within the 200-400ms time window and the 20-30Hz frequency band (talairach co-ordinates –9, 63, 51), and b) glass brain images showing the location of this voxel, and the superior frontal voxel identified as showing significant ERD associated with the target epoch within the semantic task condition for the 350-550ms time window, and 40-50Hz frequency band (talairach co-ordinates –15, 69, 33). The images show values corresponding to $-3>t>3$.

[1] Some of the significant effects identified using SnPM were placed just outside the cortical surface. There is inevitably a certain degree of experimental error and uncertainty associated with the process of MEG-MRI coregistration, and with the spatial normalization and averaging of SAM images (group SAM). The position of these activations are therefore described with respect to the nearest cortical structure within the template brain.

Later in the task prime epoch, a left superior frontal voxel was identified as showing statistically significant ERD associated with the phonological task condition (figure 7.7). This occurred within the 400-600ms time window and the 30-40Hz frequency band. A voxel at a similar location also displayed statistically significant ERD within the 30-40Hz phonological v prestimulus comparison for the target epoch (figure 7.7). This also occurred within the later time window of 500 to 700ms. The two voxels are approximately 17mm apart.

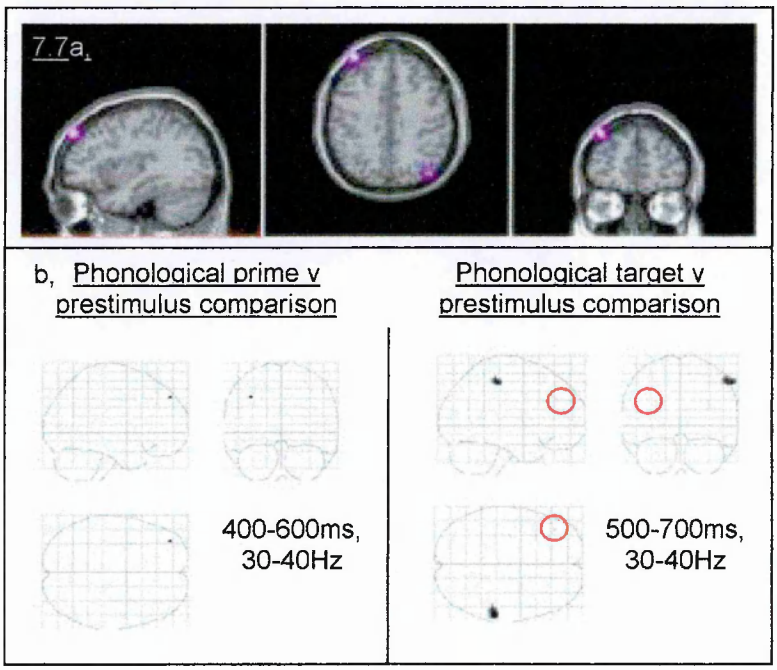


Figure 7.7. a) Images showing SnPM results for the phonological prime v prestimulus baseline comparison, within a 400-600ms time window, and a 30-40Hz frequency band. The voxel associated with statistically significant ($p<0.05$) ERD in the phonological task prime condition was localised to the middle/superior frontal gyrus, BA9/10 (talairach co-ordinates -36, 51, 42) and

b) glass brain images showing the location of this voxel, and the superior frontal voxel identified as showing significant ERD associated with the target epoch within the phonological task condition for the 500-700ms time window, and 30-40Hz frequency band (talairach co-ordinates –39, 39, 30). The images show values corresponding to $-3>t>3$.

7.3.7. Left Superior Parietal effects.

Within the 300 to 500ms time window and the 30 to 40Hz frequency band, the phonological task prime was associated with significant ERD within two left superior parietal voxels. These voxels lie in close proximity to two voxels in which significant ERD was identified in the phonological target condition, within the 350-550ms, 20-30Hz bands (figure 7.8). These voxels lie within approximately 23-30mm of each other.

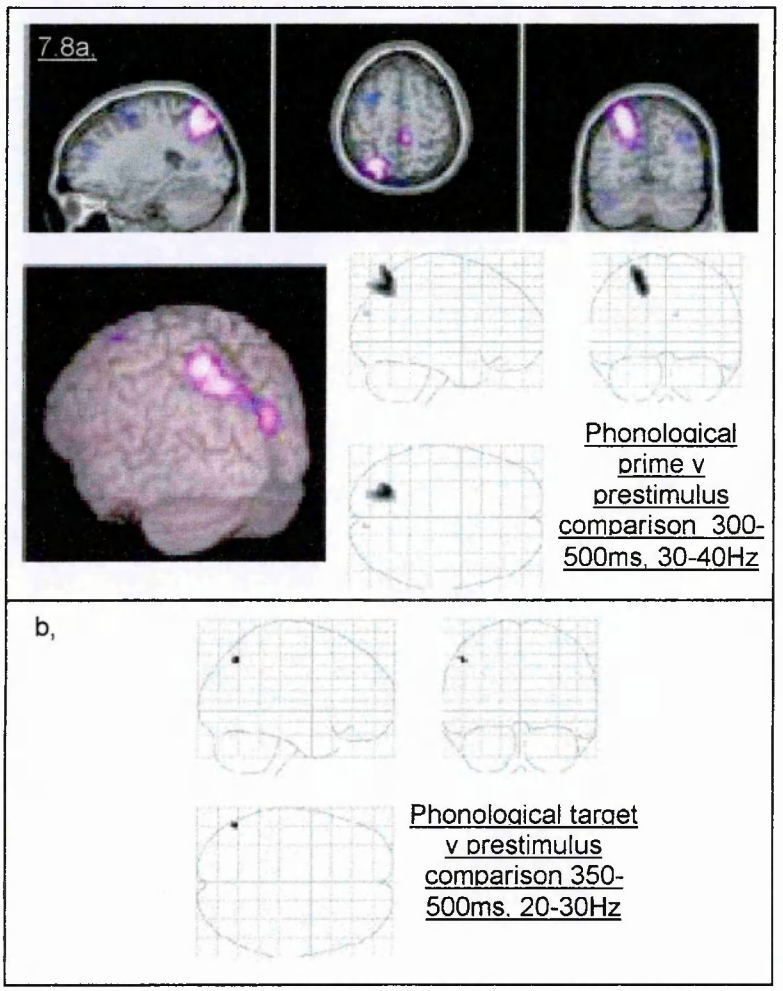


Figure 7.8. SnPM results showing a) statistically significant left superior parietal ERD associated with the phonological task prime condition, within the 300-500ms, 30-40Hz phonological v prestimulus comparison (talairach co-ordinates -24, -66, 60 and –21, -66, 48), and

b) statistically significant left inferior parietal ERD associated with the phonological target condition, within the 350-550ms time window, and 20-30ms frequency band (talairach co-ordinates -36, -48, 39 and –45, -60, 54). The images show values corresponding to –3>t>3.

7.3.8. Cerebellar effects.

Similarly, the phonological prime condition was associated with ERD in the left cerebellum (within the 300-500ms, 20-30Hz band). The phonological target condition was assoicated with significant ERD within the right cerebellum for both the 350-550ms and 500-700ms, 14-20Hz comparisons (figure 7.9).

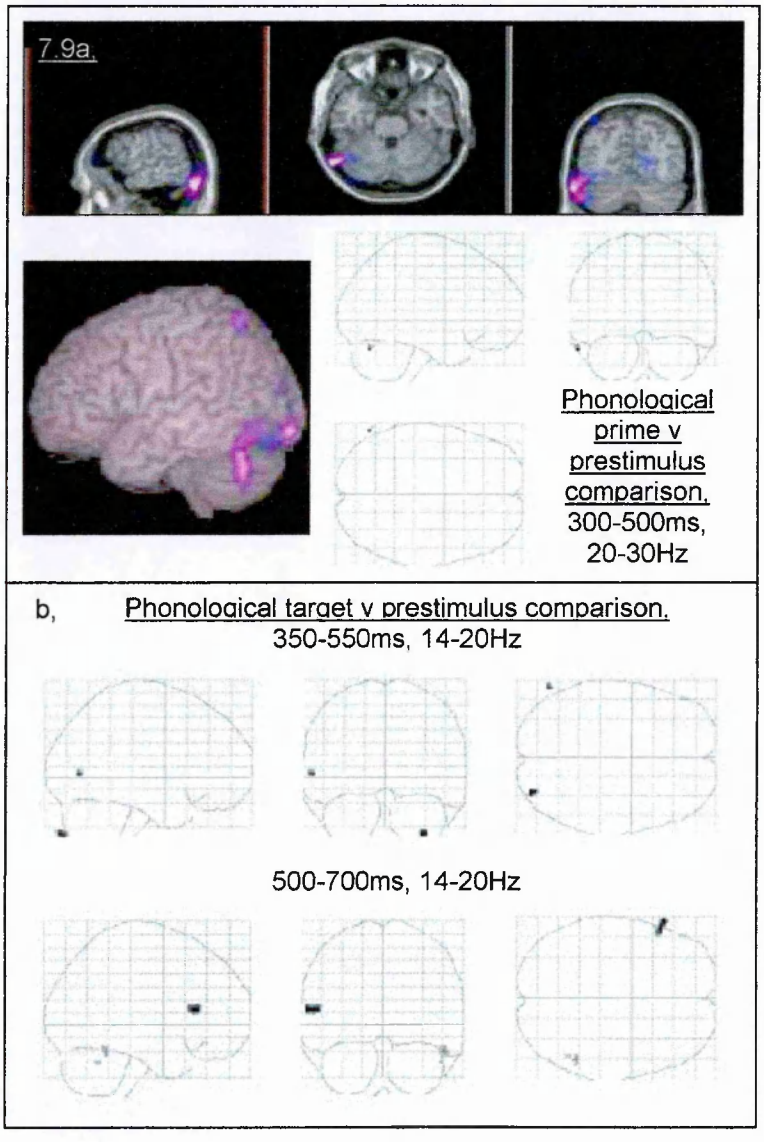


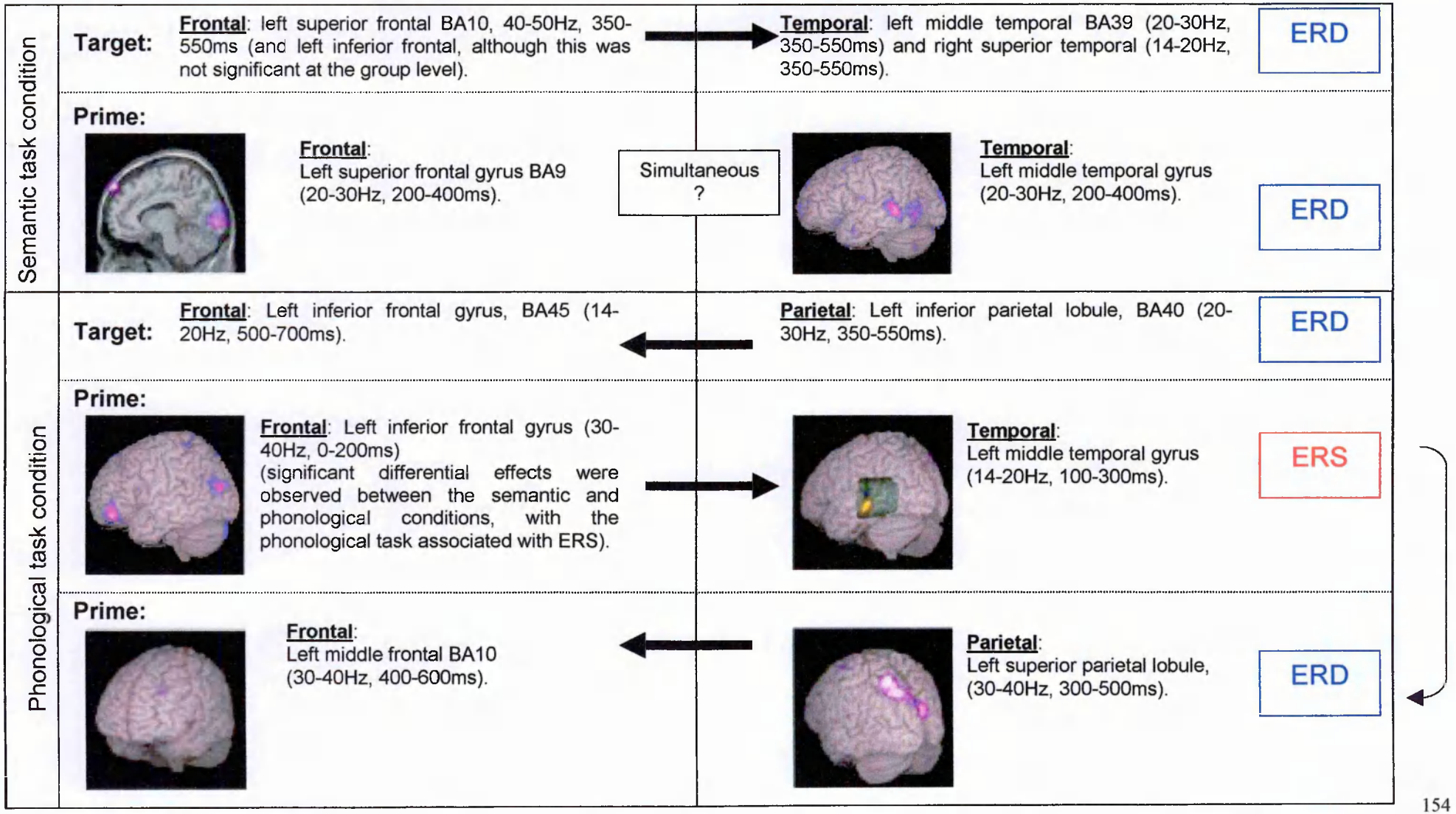
Figure 7.9. SnPM results showing a) statistically significant left cerebellar ERD associated with the phonological task prime condition, within the 300-500ms, 20-30ms comparison (talairach co-ordinates -60, -69, -27), and
b) statistically significant right cerebellar ERD associated with the phonological target condition, within both the 350-550ms, 14-20ms comparison (talairach co-ordinates 30, -87, -48) and the 500-700ms, 14-20Hz comparison (talairach co-ordinates 48, -54, -30). The images show values corresponding to –3>t>3.

7.3.9, The relative timing of frontal and temporal / parietal effects

Within the target epoch, both left inferior frontal and left superior frontal ERD preceded temporal ERD within the semantic task condition, whereas parietal ERD preceded superior frontal ERD within the phonological task condition (figure 7.10). Similarly, within the phonological task prime epoch, parietal ERD preceded superior frontal ERD. It should be noted that the ERS within the phonological condition followed the time course of the ERD observed within the semantic target condition. No consistent temporal relationship was observed between the temporal and frontal ERD observed within the semantic task prime condition, the order of these effects varied between individuals, and in most cases were effectively simultaneous.

Figure 7.10, An illustration of the spatial temporal dynamics associated with frontal and temporo/parietal ERD and ERS within the two task conditions, and both the task prime and target epochs. Whereas frontal and parietal ERD associated with the phonological task condition follows the same time course within both the task prime and target epochs, frontal and temporal ERS observed within the phonological task prime condition follows the time course of ERD observed within the semantic target word condition. The images show values corresponding to $-3>t>3$.

7.10.


Semantic task condition
Target:
Frontal: left superior frontal BA10, 40-50Hz, 350-550ms (and left inferior frontal, although this was not significant at the group level).
Temporal: left middle temporal BA39 (20-30Hz, 350-550ms) and right superior temporal (14-20Hz, 350-550ms).
ERD
Prime:
Frontal:
Left superior frontal gyrus BA9 (20-30Hz, 200-400ms).
Simultaneous ?
Temporal:
Left middle temporal gyrus (20-30Hz, 200-400ms).
ERD
Phonological task condition
Target:
Frontal: Left inferior frontal gyrus, BA45 (14-20Hz, 500-700ms).
Parietal: Left inferior parietal lobule, BA40 (20-30Hz, 350-550ms).
ERD
Prime:
Frontal: Left inferior frontal gyrus (30-40Hz, 0-200ms)
(significant differential effects were observed between the semantic and phonological conditions, with the phonological task associated with ERS).
Temporal:
Left middle temporal gyrus (14-20Hz, 100-300ms).
ERS
Prime:
Frontal:
Left middle frontal BA10 (30-40Hz, 400-600ms).
Parietal:
Left superior parietal lobule, (30-40Hz, 300-500ms).
ERD

7.4, Conclusions

The results show a number of significant effects, which are apparently related to the task-dependent priming of semantic and phonological "task sets". Significant task-dependent differential effects were identified within the task prime epoch. Also, a number of similarities were observed between these task-specific effects and those observed in response to the presentation of the target stimulus (although within the target epoch significant effects were observed only with respect to the prestimulus baseline, semantic v phonological differential effects failed to reach statistical significance at the $p<0.05$ level. The results also suggest a task-specific dissociation between ERD (within the semantic task) and ERS (within the phonological condition) in certain left medial/inferior frontal, and bilateral temporal regions. Each of these effects will be considered in turn.

7.4.1, Task-specific effects observed within the task-cue epoch

The definition of a "task set", as involving the "selection of relevant stimulus-response mappings for the upcoming task" (Brass & Cramon, 2002), together with the "switch cost" observed within task-switching studies, suggests that the presentation of a task cue will lead to a preparation process that is specific to the task that is being primed. On the basis of their fMRI results, Sakai & Passingham (2003) reported no significant task-dependant amplitude changes within the task-cue epoch, although they did observe a dissociation between the two task conditions in terms of inter-regional interactions.

The task conditions employed by Sakai & Passingham (2003) related to the order in which to recall a sequence of items (forwards or backwards). The results presented within this chapter show differences, in terms of spectral power change, between the preparation of a phonological (syllable counting) and a semantic (living/nonliving decision) task. Such differential effects were observed within left frontal, bilateral temporal, left parietal and left cerebellar regions.

7.4.2, Frontal effects

Firstly, task-dependent differential effects were observed early within the task-cue epoch (within 0-200ms of stimulus onset) within the left medial/inferior frontal region (BA10/11). This effect was observed within a voxel superior to the inferior frontal region

showing significantly enhanced activation in response to task cues priming a verbal rather than a spatial task (Sakai & Passingham, 2003, the two regions are approximately 39mm apart). Instead the voxel is closer to the anterior prefrontal region identified by Sakai & Passingham (2003) as showing enhanced activation in response to the task cue, irrespective of the task being primed. (The two regions are approximately 29mm apart). This region, however, is spatially remote (by approximately 70mm) from the inferior frontal region identified by Brass & Cramon (2002) as being "responsible for implementing a task set" (page 914).

Instead, the region identified seems to be more in line with the BA10 regions identified by studies designed to investigate the neural correlates of semantic processing, (for example, MacLeod et. al. 1998). This is also consistent with the finding of similar task-dependent BA10 effects occurring within the target epoch. Within both the pime and target epochs, ERD was observed within the semantic condition. In contrast, the phonological task was associated with ERS within this region, within both the task-cue and the target epochs. In both cases, these effects were confined to the high beta frequency band (27-35Hz). The task-dependent dissociation between ERD and ERS will be discussed later.

7.4.3, Superior frontal effects

Task-specific effects were also identified within left superior frontal regions. These regions showed significant ERD within the early time window of 200-400ms, in response to presentation of the semantic task prime. Within the later time window of 400-600ms, significant superior frontal ERD was observed within the phonological condition. This mirrors the relative latencies of significant ERD effects observed within the target epoch within the two task conditions.

Sakai & Passingham (2003) observed similar task specific differential effects within a dorsolateral prefrontal region approximately 20mm away from the voxel in which significant ERD was observed within the phonological task. However, Sakai & Passingham (2003) failed to find an involvement of this region within the epoch associated with the presentation of the task cue.

Assuming that this region plays a role in the executive control of processes such as selection and retrieval (Otten & Rugg, 2001; Davachi, Maril & Wagner, 2001), these

results suggest that task-related differences relating to the involvement of this region can be observed. Results suggest that the semantic task recruits these regions at shorter latencies compared to the phonological task. The results also suggest that task processing is not necessary for these differential effects to become apparent, and that the presentation of a task-cue priming the appropriate task gives rise to similar effects to those observed during the process of task completion.

7.4.4, Temporal effects

Task-specific differential effects were also observed within temporal regions, during the task-cue epoch. The early left middle temporal region showing this differential effect approximately coincides with that identified by Sakai & Passingham (2003) as showing enhanced activation in response to a task cue that primes a verbal task compared to a task cue that primes a spatial task. The peak of the differential effect is approximately 2mm away from that identified by Sakai & Passingham (2003). The results presented here suggest that this left middle temporal region also shows a differential effect between the presentation of a cue priming a semantic task (associated with ERD within the high beta band), and a cue priming a phonological task (associated with ERS within the low beta band). These differential effects are observed within the first 400ms of task-cue onset.

These middle temporal regions are also in close proximity of middle temporal regions identified within various studies designed to investigate semantic processing. The voxels identified within this study lie within 1cm of those identified using fMRI as showing enhanced activity during a task requiring participants to attend to relations between semantically related words, compared to an equivalent task involving rhyming words (McDermott, Petersen, Watson & Ojemann, 2003).

Significant right inferior temporal ERS was observed in response to presentation of the task prime within the phonological task condition, but not the semantic task condition, and not within the epoch associated with the presentation of the target stimulus. This effect was superior and anterior to the region identified by Sakai & Passingham (2003) as showing a differential effect between cues priming a verbal and a spatial task. The region is more in keeping with those linked to semantic processes, for example the temporal region identified by Vandenberghe et. al. (1996) in response to a task requiring participants to match stimuli according to the physical size of their referents, rather than the actual size of the stimulus. However, unexpectedly the results presented within this chapter show

significant effects (ERS) within this region, only in the phonological task condition. Possible interpretations for this will be discussed in the following section concerning the possible functional significance of ERD and ERS.

Significant differential effects were observed within right superior temporal regions, in the vicinity of the BA22 region in which Sakai & Passingham (2003) observed significant differential effects between their verbal and spatial task priming conditions, although their significant effect was observed in the left hemisphere. The voxel identified as showing significant ERS within the phonological task prime epoch (within the gamma frequency band), and ERD within the semantic target epoch (within the low beta frequency band) was approximately 20mm away from the equivalent right hemisphere location to that in which Sakai & Passingham (2003) identified significant differential effects. These results indicate that these regions may not only show "domain specificity" in response to the task cue, but also differential effects between task cues priming either a phonological or semantic task. This is in keeping with the results of studies suggesting that such regions play an important role within phonological tasks (Démonet, Fiez, Paulesu, Petersen & Zatorre, 1996; Démonet, Chollet, Ramsay, Cardebat, Nespoulous, Wise, Rascol & Frackowiak, 1992; Paulesu, Frith & Frackowiak, 1993).

7.4.5, Parietal effects

Significant left superior parietal ERD was observed within the phonological task-cue epoch. This was in close proximity to the left superior parietal (BA40) ERD observed within the phonological target epoch at a similar latency (between 300 and 550ms). Both of these effects were observed within beta frequency bands. These results are in keeping with the results of studies designed to investigate the neural correlates of phonological processing, which highlight the involvement of such parietal regions, specifically the supramarginal gyrus and BA39/40 (Paulesu et. al. 1993; Mummery et. al. 1998; Otten & Rugg, 2001). They also extend these findings to suggest that the task-specific involvement of these regions can be primed by the presentation of a task cue informing participants of a forthcoming phonological task.

7.4.6, Cerebellar effects

Similarly, statistically significant left cerebellar ERD was observed within the task prime epoch only within the phonological condition, and also within the phonological

target epoch at a similar latency (300-500ms). Both of these effects were observed within low beta frequency bands. Contrary to reports of cerebellar effects being specifically linked to semantic task conditions (Roskies et. al. 2001), these results are in keeping with the results of Mummery et. al. (1998) which show the involvement of cerebellar regions within syllable-counting tasks, and support the interpretation that these regions play a role in sub-vocalisation processes. As with the parietal effects, these results indicate that cerebellar sub-vocal rehearsal processes may be primed by the presentation of an appropriate task-cue.

7.4.7, Task specific similarities between the prime and the target

The similarities between the effects observed in response to the presentation of a task-cue and those observed in response to the presentation of a target stimulus support the notion of a task-specific "task set" being established prior to presentation of the target stimulus. Specifically, these results support the notion of distinct phonological and semantic "task sets", as suggested by (Zevin & Balota, 2000), while apparently removing the possibilities of introducing confounds associated with the time taken to read word and nonword primes, as in the "time criterion account" (Kinoshita & Lupker, 2003). These results extend this notion by showing similar task-specific macroscopic neural effects in response to the task cue to those observed during task completion.

7.4.8, Possible confounds

Although the use of single word task instructions to prime semantic and phonological "processing pathways" may avoid the confounds associated with the use of nonwords to prime a phonological/sublexical pathway, and exception words to prime a lexical/semantic pathway (as within the paradigm employed by Zevin & Balota, 2000), the possibility of there being confounds associated with the choice of task cues can not be ruled out. For example, the task primes for the two conditions differed in terms of the nature of their referents (ie. semantic categories in the case of the semantic task, and numbers in the case of the phonological task), and word length (task-cues were longer in the case of the semantic task condition). However, there a number of reasons why it seems unlikely that such differences could fully account for the differential effects observed.

Firstly, there were a number of instances in which the effects observed within the task-cue epoch were mirrored within the epoch in which the target stimulus was presented.

For example, it is possible to speculate that differences relating to the choice of task cues may have lead to the latency difference associated with significant superior frontal ERD between the two conditions. However, not only was this effect observed later within the phonological condition, (which employed shorter task cues than within the semantic condition, both in terms of number of letters and number of syllables), but this latency difference was mirrored within the target epoch. It seems unlikely that effects observed within this epoch could be accounted for in terms of such confounds, as the same target stimuli appeared within each condition.

It is also possible to speculate that differences in terms of the strength of the association between the task cues and the tasks they were used to prime may have contributed to such differential effects. For example, Arbuthnott & Woodward (2002) argue that task cues which have long-standing associations with certain tasks may bias the appropriate response options to a greater degree than a task cue that has no prior association with a specific task. It would seem reasonable to assume that the task cues employed within the semantic condition (i.e. "living?" and "nonliving?") may be more strongly associated with the living/nonliving judgement task, than the task cues employed within the phonological task (i.e. "one?" and "two?") are with the syllable counting task. However, very different significant effects were observed within the task-cue epoch for the two conditions, compared to the prestimulus baseline. These task-specific effects were also closely allied to the literature concerning the neural correlates of semantic and phonological processing. This suggests that the differential effects associated with the priming of the two tasks arose due to task-specific differences in the process of task preparation, rather than an enhanced priming effect for one task condition relative to the other.

7.4.9. Dissociation between ERD and ERS and the two task conditions

Whereas each of the significant effects observed within the semantic condition took the form of power decreases (indicative of ERD), significant power increases (ERS) were observed in the phonological condition within left inferior frontal, left middle temporal, right inferior temporal and right superior temporal regions. These results suggest a task-related dissociation between ERD and ERS within semantic and phonological task priming conditions, although the reason for this effect is unclear.

As outlined in Chapter 2, ERD has been described as a "correlate of an activated cortical area (Pfurtscheller, 2001, page 1257), observed within a range of cognitive paradigms (Dujardin, Bourriez & Guieu, 1995; Singh et. al. 2002) and found to coincide with regions showing an evoked haemodynamic response using fMRI (Singh et. al. 2002), supporting the notion that ERD represents increased neural activation in a cortical area.

In contrast, ERS has been described as the "correlate of a deactivated cortical area" (Pfurtscheller, 2001, p1257), and indicative of "cortical areas at rest or in an idling state" (Karrasch et. al. 1998, p112) or a state of functional inhibition (Klimesch, 1996; Neuper & Pfurtscheller, 2001).

There are a number of reasons why the beta and gamma ERS effects observed within this study would fit an account whereby ERS represents inhibition. Firstly, the left inferior frontal, left middle temporal and right inferior temporal regions, in which ERS was observed within the phonological task, are typically associated with semantic processing (McDermott et. al. 2003; MacLeod et. al. 1998). Furthermore, within the left inferior frontal gyrus, significant ERD was observed within the semantic condition at very similar latencies and frequencies to those at which significant ERS effects were observed within the phonological task condition (within both task-cue and target epochs). Similarly, significant ERD was observed in the target epoch of the semantic task condition within the right superior temporal region, and significant ERS was observed within this region during the phonological task-cue epoch (although in this case the latencies and frequency bands differed).

Finally, the relative timing of ERD and ERS effects observed within frontal and temporal "stores" (in the case of the semantic task) and parietal "stores" (in the case of the phonological task), also support this interpretation. Whereas frontal ERD precedes temporal ERD within the semantic task cue epoch, parietal ERD precedes frontal ERD within both the task cue and the target epochs. However, the ERS observed within temporal and left inferior frontal regions during the phonological task cue epoch follows the relative time course of the ERD within the semantic task cue epoch. This also seems to support the notion that ERS within the phonological condition reflects inhibition of semantic processes, both in terms of the regions involved, and the time course of the effects.

These similarities seem to support the hypothesis that ERS observed within typically semantic regions, but within the phonological task condition, may represent the inhibition of semantic processes.

However, as outlined in Chapter 2, there are a number of problems associated with interpreting ERD and ERS effects in such phenomenological terms. Although, as the name suggests, ERS has been described as resulting from "the cooperative or synchronised behaviour of a large number of neurons" (Pfurtscheller & Lopes da Silva, 1999, p1852), and ERD as desynchronised behaviour, it has been argued that such a model represents an oversimplification, and fails to explain a number of macroscopic oscillatory effects (Hadjipapas & Barnes, in preparation). In particular, the "cortical idling" interpretation of ERS is criticised based on findings such as those showing occipital alpha ERS to covary and increase in terms of spectral power with increasing task demands (Krause et. al. 1996; Jensen et. al. 2002).

Karrasch et. al. (1998), for example, reported significant alpha ERS in response to the presentation of a stimulus which was preceded by the presentation of a pseudoword. The authors suggest that the ERS may "reflect the phonological processing of the stimulus" (p119). Similarly, alpha ERS has been observed in response to the auditory presentation of a sequence of vowels which were to be remembered (Krause, et. al. 1996), and linked to the facilitation of auditory stimulus processing (Tiihonen, Hari, Kajola, Karhu, Ahlfors & Tissari, 1991).

One interpretation that may account for the reports of ERS within phonological task conditions, but not within semantic task conditions, may be that semantic representations involve larger cortical areas (Karrasch et. al. 1998), comprising a greater number of regionally and functionally distinct clusters, which leads to the observation of ERD at the macroscopic level. Conversely, phonological processing may involve fewer of these clusters, and therefore show ERS at the macroscopic level, even when phonological processes are being primed, as in the case of this study. This interpretation is in keeping with reports of ERS being observed during phonological tasks (for example, Krasue et. al. 1996; Karrasch et. al. 1998). Although, unlike the ERS reported within these studies, ERS identified within the present study was observed within beta and gamma frequency bands. Gamma ERS has been interpreted as representing a process of binding sensory information (Pfurtscheller & Lopes da Silva, 1999), so it is also possible to speculate that such a process may play a role in the phonological processing of visually presented words.

To conclude, although a number of observations fit an interpretation of ERS as representing inhibitory processes, it seems likely that the apparent task-specific dissociation between ERD and ERS effects, as observed within this study, can only be fully understood once more is known about the functional organisation and the dynamics of the underlying neuronal networks.

7.4.10, Summary

The preparation of semantic and phonological task processing was investigated using the presentation of task cues. MEG data revealed a number of statistically significant differential effects between the two task conditions, in response to the presentation of a task cue. In keeping with the notion of task set preparation, parallels were identified between the task specific effects associated with the presentation of the task cue, and those associated with the presentation of the target stimulus (although differential effects observed as a result of a direct semantic v phonological comparison only reached statistical significance within the task prime epoch, not within the target epoch). It could be speculated that the presentation of the task prime prior to presentation of the target stimulus may account for the semantic v phonological effects failing to reach statistical significance during the target epoch. This could be tested by devising an experiment in which tasks were not primed in this way.

In response to the presentation of the task cue, a task specific ERD/ERS dissociation was observed within the left middle temporal gyrus and left inferior frontal gyrus, with the semantic task condition associated with ERD and the phonological task condition associated with ERS. The functional significance of this dissociation is unclear.

Chapter 8

The use of stimulus manipulations in the study of the neural correlates of semantic and phonological processing.

8.1, Psychological models

As mentioned within the previous chapters, various authors have suggested stages, or "separable subprocesses" (Friederici, Opitz & Yves von Cramon, 2000) which the analysis of visually presented single word stimuli may involve. The concept of processing-levels has been incorporated into a number of theories (Bentin, Mouchetant-Rostaing, Giard, Echallier & Pernier, 1999), although the proposed stages tend to differ among authors. Dehaene (1995) summarizes neuropsychological models of lexical access as tending to involve three stages, visual analysis of stimulus shapes, construction of a structural representation of the letter string (visual word form), and access to lexical and semantic information. Bentin et. al. (1999) also describe a three-stage model of recognising printed words, which involves orthographic, lexical, and semantic processing. Other stages have been suggested such as "feature detection" (Halgren, Baudena, Heit, Clarke, Marinkovic, 1994a), integration of features into an orthographic pattern, and phonological representation (Dehaene, 1995).

Chapters 5 and 7 consider studies in which task manipulations have been used to investigate semantic and phonological processes. An alternative approach to investigating such processes is to use stimulus manipulations. For example, the processing of consonant strings has been contrasted with the processing of symbol strings, in order to investigate orthographic processes (e.g. Tarkiainen, Helenius, Hansen, Cornelissen & Salmelin, 1999). Phonological processes have been investigated by contrasting the processing of pronounceable nonwords with that of nonpronounceable nonwords (Bentin et. al. 1999). The processing of real words has been contrasted with the processing of pronoucable nonwords in order to investigate lexical/semantic processes (Bentin et. al. 1999).

8.2, Evoked response results

Such stimulus manipulations have been employed within evoked response studies, whereby attempts have been made to match the proposed subprocesses to different evoked response components. The results of such attempts have by no means been conclusive. In 1996 it was claimed that although "several ERP components related to language processing

have been described, the language specificity of the different ERP components is still under discussion" (Eulitz, Maess, Pantev, Friederici, Feige, & Elbert, 1996). This seems to apply to the ERP components evoked by visually presented single words, with recent articles in which authors such as Schendan, Ganis, & Kutas (1998) still apparently offer alternative interpretations of observed ERP components.

8.3, Sensory analysis

Psychological models tend to incorporate an initial "sensory analysis" stage, which is not thought to be "word specific", but dependent instead upon simple image properties. Schendan et. al. (1998) attempted to relate this stage to observed neural activity by presenting participants with various visual stimuli, line drawings of familiar objects, line drawings of "pseudo-objects", concrete nouns, "nonwords" constructed from random sets of letters, "pseudofont" strings and "icon strings" constructed from simple line drawings of objects. Participants were required to passively rate how much they liked each image, while only responding overtly when presented with a cue. Schendan et. al. (1998) found that by 90ms occipital ERPs appeared to differentiate between word and "wordlike strings" versus faces and other objects. Because of their early latency, and inability to differentiate between words and "wordlike strings" (words, nonwords and pseudofont strings), it was concluded that these occipital differences did not specifically reflect differences between linguistic and non-linguistic stimuli. Instead they were believed to result from differing low-level visual properties such as aspect ratio and spatial frequency (Schendan et. al. 1998).

Tarkiainen et. al. (1999) identified such early visual analysis in a latency range of ~80-130ms. They labelled this "type1 activation". Participants were presented with various types of stimuli including pure noise, single letters, two letter syllables, four letter words, and symbol strings which consisted of strings of distorted text. Equivalent Current Dipoles (ECDs) were plotted in 12 subjects. ECDs that fulfilled "type1" criteria were found in 10 of these subjects, and originated in occipital areas bordering V1 and extending laterally as far as V4. "Type 1" sources did not show object-specificity as the amplitudes were the same for letter and symbol strings of equal length but type 1 activation did increase with increasing length of string, irrespective of string type. It was concluded that this Type 1 activity reflects low-level processing that is common to all visual stimulus types.

8.4, P150

It has been suggested that a posterior fusiform evoked response component at approximately 150ms may show word-specificity (Schendan et. al. 1998), whilst being unaffected by low-level visual properties such as string length and aspect ratio. Schendan et. al. (1998) reported that a broadly distributed, bilateral positivity, which was maximal around 155ms (the P150), was much more positive to "word-like" than "object-like" images. However, icon-strings evoked a positivity that was intermediate to that evoked by the other two stimulus categories. The authors explained these findings by suggesting that icon-strings are both "word-like" and "object-like". However, it would seem that iconstrings were similar to both "word-like" and "object-like stimulus types only in terms of general visual form. Iconstrings had no similarity to words in terms of linguistic content. This would suggest that instead of being word-specific, the P150 might, in some way, index the extent to which the overall form of the stimulus resembles that of a word.

The finding of similar effects evoked by face stimuli, also within the posterior fusiform gyrus (Schendan et. al. 1998), again challenges the suggestion that the P150 may be word specific. These findings indicate that the P150 may not be dependent solely upon the visual stimulus being linguistic, or even resembling a word form. As a possible feature specific to words and faces Schendan et. al. (1998) suggest that it may be the familiarity of the visual image that is indexed by the P150.

8.5, N200

Allison, McCarthy, Nobre, Puce & Belger (1994) report having found a component, which appeared to differentiate between "word-related" stimuli and faces. As a result of their depth-electrode study, a negative potential, N200, was recorded from regions of the fusiform and inferior temporal gyrus. The "word-related" N200 was evoked equally by content words, legal and illegal nonwords, so was thought to show letter-specificity. Although face and letter-string N200s were similar in waveform and were recorded from the same regions, the letter string N200s were typically shorter in peak latency by about 30ms. Also, electrodes that recorded a letter-string N200 did not necessarily record a face N200. These findings led the authors to conclude that there is "anatomical and functional specificity of "letter-string modules" in extrastriate cortex" (Allison et. al. 1994, page 549).

Similarly, Nobre, Allison & McCarthy (1994) recorded field potentials directly from the inferior temporal lobe, and reported an N200 elicited in discrete regions of the posterior fusiform gyrus by various types of letter string (grammatical function words, nouns, pronounceable nonwords and non-pronounceable nonwords), but not other stimuli (pictures of faces, digitally scrambled faces, cars and digitally scrambled cars).

As a result of a MEG study conducted by Eulitz, Eulitz, Schaeffer, Kelepir & Marantz (2000) an M180 component of evoked magnetic field was found to be larger for the processing of word and false font stimuli compared to shape and dot patterns. As the original letters used to derive the false font stimuli could be easily recognised, it could be argued that these findings support the claim that orthographic processing is indexed by a component at approximately 200ms.

8.6, N320

In order to interrogate a phonological stage of processing, Bentin et. al. (1999) measured ERPs elicited by words, pseudowords and consonant strings during a rhyming task. Although it has been suggested that processing consonant strings may involve a certain amount of phonological processing (Bokde, Tagamets, Friedman & Horwitz, 2001), it was assumed that phonological processing associated with words and pseudowords would differ significantly from that associated with consonant strings. Findings reveal an N320 component that appeared to differentiate between pronounceable and non-pronounceable stimuli. Pronounceable stimuli produced an N320 with a larger amplitude over left temporal areas than non-pronounceable stimuli.

8.7, N400

Various studies have compared the processing of words or nonwords believed to require little or no semantic processing, with semantically meaningful words, in order to identify the neural correlates of a possible semantic processing stage, often described as the final stage of visual word processing (Dehaene, 1995; Bentin et. al. 1999). For example, Nobre et. al. (1994) report a depth electrode study in which a P400 component was found to be larger for words with semantic content than for grammatical function words. The P400 was diminished by semantic context, and not elicited by nonwords or faces. It was therefore concluded that the P400 reflected activation of the "word concept". A number of

authors have reported an N400 component which appears to be sensitive to semantic manipulations (Gomes, Ritter, Tartter, Vaughan & Rosen, 1997).

8.8, Problems associated with relying on evoked response analysis

There are a number of problems associated with these studies. Firstly, evoked responses must be both time-locked and phase-locked to stimulus onset. It has been argued that higher level cognitive processes, such as language processes, are inherently variable, and therefore poorly phase-locked to the stimulus across trials (Michalewski, Prasher & Starr, 1986). The frequency specific changes in cortical oscillatory power that can be investigated using SAM can either be evoked (phase-locked to the stimulus), or induced by the presence of the stimulus (without phase-locking). It therefore seems to be particularly advantageous to adopt this approach when investigating linguistic processes.

8.9, Interpretation difficulties

Another feature of the studies described is that they assume that the presentation of a certain type of stimulus affords the type of processing to which they are best suited. For example, by comparing letter strings with other types of stimuli it was believed that the process of "orthographic processing" could be isolated (Allison et. al. 1994; Nobre et. al. 1994). Similarly, the presentation of pronounceable nonwords was assumed to afford phonological processing, whereas the presentation of nonpronounceable nonwords was not (Bentin et. al. 1999).

However, Specht, Holtel, Zahn, Herzog, Krause, Mottaghy, Radermacher, Schmidt, Tellmann, Weis, Willmes & Huber (2003) adopt a different approach by considering the presentation of different stimulus types within the context of a lexical decision process. Although they specifically refer to auditory stimulus processing, their arguments seem to also be applicable to visual stimulus processing. They state that performing a lexical decision on a phonologically incorrect nonword mainly involves a phonological discrimination process, whereas performing a lexical decision on pronounceable pseudowords mainly requires a process of lexical access. Specht et. al. (2003) report the results of PET study which apparently support this interpretation (which will be discussed in the following section).

The involvement of phonological processes in the processing of nonpronounceable nonwords is also predicted by the "universal direct access hypothesis" (for example, as outlined within the model proposed by Ans, Carbonnel & Valdois, 1998). Such an approach asserts that reading involves initial global processing where the familiarity of a string is assessed, and if it is unfamiliar then attempts are made to extract it's phonological counterpart.

In this way the results of imaging studies that have used such stimulus manipulations have been interpreted in very different ways. Mechelli, Gorno-Tempini & Price (2000) consider this problem specifically with regard to the interpretation of studies which involve the presentation of words and pseudowords to investigate semantic and phonological processing. They state that a double dissociation in the activation patterns from reading words and pseudowords could either reflect "a) differential demands on lexical and sublexical routes; or b) the degree to which semantics and phonology is activated for words and pseudowords, respectively" (Mechelli, Gorno-Tempini & Price, 2003, page 268). The investigation reported within Chapter 9 employed the use of a lexical decision task in an attempt to constrain the processing involved, although the study still suffers from interpretation ambiguities.

8.10, Pseudowords

Mechelli et. al. (2003) conducted a review of various PET and fMRI studies in which pseudoword reading was compared to real word reading. As a result of this review the most consistent effects observed in response to pseudowords relative to real words were reported within the left inferior frontal gyrus (for example, Xu, Grafman, Gaillard, Ishii, Veg-Bermudez, Pietrini, Reeves-Tyer, DiCamillo & Theodore, 2001; Paulesu et. al. 2000; Brunswick et. al. 1999; Fiez, Balota, Raichle & Petersen, 1999; Hagoort et. al. 1999; Herbster, Mintun, Nebes & Becker, 1997), and the inferior temporal gyrus (for example, Xu et. al. 2001; Paulesu et. al. 2000; Brunswick et. al. 1999; Price, Wise & Frackowiak, 1996). As a result of a PET study Mechelli et. al. 2003 report enhanced rCBF effects during pseudoword reading compared to real word reading within each of these regions, and also within the right cerebellum. Right cerebellar pseudoword effects were also observed within two of the studies reviewed (Hagoort et. al. 1999; Xu et. al. 2001).

Mechelli et. al. (2003) interpret these results in terms of an increased demand on lexical processing made by pseudowords. The authors argue that these three regions have

also been identified by studies designed to investigate the neural correlates of lexical retrieval, irrespective of stimulus modality, such as studies involving picture, letter and colour naming (Price & Friston, 1997), word generation (Frith, Friston, Liddle & Frackowiak, 1991a) and Braille reading (Büchel, Price & Friston, 1998).

8.11, Left inferior frontal effects

Specht et. al. (2003) used a similar approach to that taken by Mechelli et. al. (2003) to interpret the results of a PET study in which participants were required to perform a lexical decision task on various types of auditory stimuli. Higher rCBF within BA47, adjacent to Broca's area, during the processing of pseudowords, was interpreted as reflecting a strong reliance on the process of lexical access.

Herbster, Mintun, Nebes & Becker (1997) investigated the effects of pseudoword reading together with the effects of reading regular and irregular real words. Within both the irregular word and pseudoword condition, but not the regular word condition, left inferior frontal activation was observed. The authors conclude that the involvement of this region reflects enhanced phonological processing. In the case of irregular words this was believed to be due to competition between the semantic and phonological reading pathways, and in the case of nonwords due to their having been no prior experience of phonologically processing these stimuli. Similarly, as a result of a PET study reported by Xu et al (2001), word rhyming was found to activate the same brain regions engaged in pseudoword rhyming, although pseudoword rhyming induced the largest change in cerebral blood flow and activated more voxels within the left posterior prefrontal regions.

It could be argued that the reading and rhyming tasks employed within the studies reported by Herbster et. al. (1997) and Xu et. al. (2001) respectively specifically required phonological stimulus processing. Madden, Langley, Denny, Turkington, Provenzale, Hawk & Coleman (2002) describe the results of a PET study which involved various comparisons between a lexical decision task condition, and a condition involving a simple visual search task. The stimuli consisted of real words and pronounceable nonwords. Although, the analysis failed to differentiate between the two stimulus categories, the lexical decision task was associated with activation within the left inferior frontal gyrus, with local maxima within BA45 for younger adults, and BA44 for older adults. In order to interpret these results the authors consider the results of studies involving task manipulations (in this case Fiez, 1997), which indicate an involvement of posterior

prefrontal regions (e.g. BA 44 and BA45) within phonological tasks, and an involvement of more anterior regions (e.g. BA47 and BA10) within semantic tasks (as discussed within Chapter 4). Using this information to interpret the results of their study, Madden et. al. (2002) state that the prefrontal activation is more likely to reflect phonological processing within the lexical decision task.

Had the same criteria been used in the interpretation of the results presented by Mechelli et. al. (2003) and by Specht et. al. (2003), in which more anterior left inferior frontal regions were implicated in the processing of pseudowords, it is likely that these regions would have been more closely linked to the results obtained from semantic/lexical task conditions. The region of activation observed by Herbster et. al. (1997) in response to the presentation of pseudowords was larger than that observed in response to irregular words, and included both BA47 and BA44. However, it is unclear how the reading task used within this study, as opposed to the lexical decision task, may have influenced these results. Although, even when only the results of lexical decision studies are considered, there seems to be a great deal of inconsistency, as acknowledged by Mechelli et. al. (2003).

8.12, Inferior temporal effects

As a result of their review, Mechelli et. al. (2003) also identify various inferior and middle temporal regions which have been associated with the processing of pseudowords as opposed to real words. The left posterior inferior temporal region was most consistently reported to show enhanced activation in response to the presentation of pseudowords (e.g. Price et. al. 1996; Brunswick et. al. 1999; Paulesu et. al. 2000; Xu et. al. 2001). From the results of their PET study, Mechelli et. al. (2003) reported enhanced left posterior inferior temporal activation in response to pseudowords. They interpret the enhanced left posterior inferior temporal activation as reflecting enhanced demands on lexical retrieval within the pseudoword condition. Similarly, Herbster et. al. (1997) relate their observation of enhanced left fusiform rCBF during pseudoword reading to reports linking this region to semantic processing (in this case, Bookheimer et. al. 1995, as discussed within Chapter 4).

8.13, Right cerebellum

The enhanced right cerebellar activation reported by Mechelli et. al. (2003) during the processing of pseudowords relative to real words has not been as consistently linked to lexical processes as the other two effects. Mechelli et. al. (2003) suggest that the

involvement of the right cerebellum within pseudoword processing may have previously been overlooked due to right cerebellar effects being subtle, but speculate that the effects may have become apparent as a result of their analysis due to consistency among participants. Similarly, Xiang et. al. (2001) report weak cerebellar effects associated with viewing words relative to symbol strings which were apparent within each of their six participants.

As discussed in Chapter 4, whilst cerebellar effects have been linked to the process of subvocal rehearsal within a sustained search (Desmond et. al. 1998), right cerebellar effects have also been specifically linked to semantic tasks when these were compared to phonological tasks (Roskies et. al. 2001), and are apparently functionally linked to left inferior frontal effects during semantic processing (Raichle et. al. 1994; Desmond et. al. 1998). Therefore the involvement of the right cerebellum in pseudoword processing is consistent with two possible interpretations, as either being linked to phonological processes or semantic processes.

8.14, Parietal effects

Although Mechelli et. al. (2003) do not identify inferior or superior parietal regions as consistently showing enhanced activation in response to the presentation of pseudowords, Henson, Price, Rugg, Turner & Friston (2002) report a significantly enhanced and delayed BOLD response within bilateral parietal regions (specifically BA40) within the nonword condition of a lexical decision task. Unlike the studies reviewed by Mechelli et. al. (2003), the nonword condition reported by Henson et. al. (2002) included both pronounceable pseudowords and nonpronouncable nonwords. Henson et. al. (2002) use the results of studies comparing semantic and phonological tasks in order to interpret their results. Such studies (for example, Mummery et. al. 1998, as discussed in Chapter 4) suggest an involvement of these regions in phonological processes.

Henson et. al. (2002) also report enhanced right inferior frontal and temporo-occipital activation within the nonword condition which they again relate to the process of phonological retrieval. The discrepancy between these results and those reported by Mechelli et. al. (2003) could perhaps be attributed to the inclusion of nonpronounceable nonwords within the nonword condition reported by Henson et. al. (2002). This would support the claim that performing a lexical decision on a phonologically incorrect nonword is mainly based on a phonological discrimination process (Specht et. al. 2003).

As a result of an fMRI study, Owen, Borowsky & Sarty (2004) report left inferior parietal activation (BA40) in response to the presentation of pseudowords. However, rather than making a lexical decision, within this study participants were required to overtly name the stimuli, or perform a rhyming task, which may have involved phonological processes to a greater extent than a lexical decision task. Furthermore, activation within this region was enhanced within the rhyming decision task, compared to the overt naming task, supporting the hypothesis that the involvement of these left parietal regions may be modulated by phonological processing demands.

8.15, Superior temporal effects

It may also be possible to apply the same logic to superior temporal results. Consistent superior temporal effects were not reported by Mechelli et. al. (2003) within their review of pseudoword studies, and within their PET study in which left superior temporal activation was observed in response to both words and pseudowords. However, Specht et. al. (2003) reported significant effects within bilateral superior temporal regions when comparing the auditory presentation of nonwords to the presentation of tones. These seem to coincide with regions showing enhanced activation within phonological processing tasks (for example, Paulesu, 1993; Isahai, Takeuchi & Kuriki, 2000), which may suggest a reliance on phonological processes when performing a lexical decision on nonpronouncable nonwords. Specht et. al. (2003) does report similar, although less pronounced, effects within a pseudoword condition, although the extent to which the auditory stimulus presentation may have affected these results is unclear.

Conversely, Henson et. al. (2002) reported an increase in the BOLD response within left superior temporal regions in response to words compared to nonwords. However, these results may have been influenced by the inclusion of both pronounceable pseudowords and nonpronouncable nonwords within the nonword condition. Unlike Mechelli et. al. (2003), Herbster et. al. (1997), reported enhanced left superior temporal activation during the reading of pseudowords. Unlike the reading task employed by Mechelli et. al. (2003), within the task used by Herbster et. al. (1997) participants were required to read the words and nonwords aloud, which may have required a greater involvement of phonological processes.

Therefore, while there appears to be a certain degree of inconsistency regarding left superior temporal results reported by stimulus manipulation studies, investigating these effects within a lexical decision task that does not require the phonological processes associated with reading aloud, and differentiating between pronounceable and nonpronounceable nonwords, may produce clearer findings. Adopting this approach may help to clarify whether left superior temporal regions show a greater involvement in performing a lexical decision task on nonwords as opposed to pseudowords and real words.

Chapter 9

Study 3: An MEG investigation of the neural correlates of word and nonword processing within the context of a lexical decision task.

9.1, Abstract

Chapters 5 and 7 report studies in which the neural correlates of semantic and phonological processing were investigated using task manipulations. A number of authors have used stimulus manipulations in order to study these effects. Within such studies word processing has been compared with the processing of different types of nonwords, for example, symbol strings which have no orthographic, phonological or semantic component, non-pronouncable nonwords which are orthographic but have no recognisable phonological or lexical/semantic component, and pronounceable pseudowords which can be processed phonologically, but have no lexical/semantic component.

There are a number of problems associated with these studies. Firstly, most have examined only evoked responses (which are phase locked to stimulus onset), and are therefore susceptible to distortion and attenuation due to individual variability. The majority also rely on the assumption that certain stimulus types will automatically afford the type of processing to which they are most readily susceptible, regardless of the task conditions. For example, pronounceable pseudowords have been assumed to afford enhanced phonological processing, whereas the presentation of real words are thought to automatically induce lexical/semantic processing. An alternative approach considers these processing components within the context of a lexical decision process, and asserts that performing a lexical decision on pronounceable pseudowords mainly involves lexical/semantic discrimination processes, whereas performing this task on non-pronounceable nonwords mainly involves phonological discrimination processes.

Within the studies reported in this chapter participants were required to perform a lexical decision task using six different stimulus types, three were word categories and three were nonword types (pronounceable pseudowords, nonpronouncable consonant strings, and strings of symbols). By using MEG and SAM analysis, it was not only possible to investigate the time course of such processes with millisecond resolution, but also, by measuring frequency specific changes in cortical oscillatory power, it was possible to study ERD and ERS effects that are not necessarily phase-locked to stimulus onset (induced). This may be particularly advantageous in a cognitive paradigm such as this.

By using a lexical decision task an attempt was made to avoid the confounds associated with task requirements such as reading aloud, which may bias phonological processes. However, the use of this task does not exclude the possibility of confounds being introduced, for example, Henson et. al. (2002) stated that word-nonword differences in a lexical decision task could reflect the different decisions (acceptance versus rejection) rather than differences in stimuli per se. It was also believed that the use of a lexical decision task would remove the need to rely on the assumption that the presentation of a certain stimulus type automatically affords a certain type of processing. In a further attempt to overcome the interpretation difficulties discussed previously, a behavioural study was conducted in order to determine mean reaction times for the different stimulus conditions. The MEG data can therefore be interpreted within the context of these reaction time constraints.

MEG results reveal differential effects depending on the "word like" nature of the stimulus within right cerebellar, bilateral parietal, inferior and superior temporal and middle frontal regions. The primary aim was to investigate differences associated with the "word like" nature of the stimulus (i.e. between the different non-word conditions), differences between the word conditions are beyond the scope of this thesis. Attempts were made to interpret the MEG data within the context of the reaction time data, the results of previous task manipulation studies, and the results of the task manipulation studies reported in Chapters 5 and 7. The most consistent effect was observed within bilateral inferior temporal regions, where less "word-like" stimuli tended to be associated with enhanced ERD within the beta frequency range. These inferior temporal regions have often been associated with semantic processing, and described as representing "semantic stores", so that the enhanced beta ERD may reflect a greater reliance on lexical/semantic discrimination processes when conducting a lexical decision on less "word-like" stimuli. The functional significance of superior temporal, parietal, right cerebellar, and left middle frontal effects is ambiguous, which may be due to the many methodological problems associated with the use of stimulus manipulations.

9.2, Behavioural Study: Introduction

In an attempt to aid interpretation of the MEG data, mean reaction times were determined for performance of the lexical decision task on each of the stimulus types. As a cued response was used within the MEG study, in an attempt to keep the motor response separate from stimulus processing, reaction time data was not acquired during the MEG experiment, but within a separate behavioural study.

9.3, Behavioural Study: Method

9.3.1, Participants

Twenty-four participants gave informed consent to participate in this study (6 males and 18 females). Participants were undergraduate psychology students, and all stated English as their native language. All had normal, or corrected-to-normal vision.

9.3.2, Stimuli

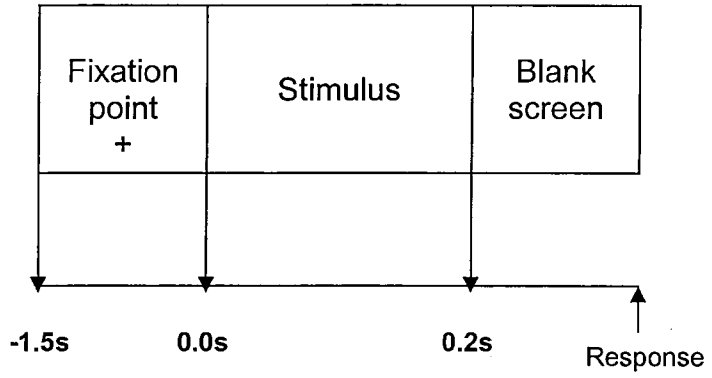
The stimuli consisted of 180 images; 90 words and 90 nonwords. Within the word category there were 30 abstract nouns, 30 concrete nouns, and 30 homographs. Homographs were defined as words that have two or more semantically independent meanings, but one pronunciation. Each word contained either five or six letters, and had a minimum word familiarity rating of 450 (MRC Psycholinguistic database, 1987, overall range 100-700, mean score 488). Abstract words had a maximum concreteness score of 440 (MRC Psycholinguistic database, 1987, overall range 100-700, mean score 438) and a maximum imagability rating of 450 (MRC Psycholinguistic database, 1987, overall range 100-700, mean score 450).

The nonwords were 30 pseudowords, 30 consonant-strings, and 30 symbol-strings. Pseudowords were defined as nonwords that are phonologically plausible. An attempt was made to limit the similarity between pseudowords and real words by ensuring that each pseudoword could not be changed into an easily recognisable real word by the substitution of a single letter. Symbol strings comprised of non-alphanumeric symbols, which were mostly punctuation symbols. Nonwords contained five or six letters or symbols. All letters and symbols were of a standard size and font, and were black on a white background.

9.3.3, Procedure

Participants viewed a computer monitor which initially displayed a red fixation point in the centre. Following this the words and nonwords were presented in pseudo-random order, in the centre of the screen. Each string was displayed for 200ms, and then the screen was blank until a response was made. Participants were asked to decide whether each string was a word or a nonword and indicate their response by pressing one of two buttons. Reaction time data was recorded. The stimulus sequence is shown in figure 9.1.

Figure 9.1, The stimulus sequence



9.4, Behavioural Study: Results

The mean reaction times for each of the stimulus categories are presented in figure 9.2. From this graph it can been seen that out of the six stimulus categories, participants tended to respond to the lexical decision task fastest when presented with symbol strings, and slowest when presented with pseudowords.

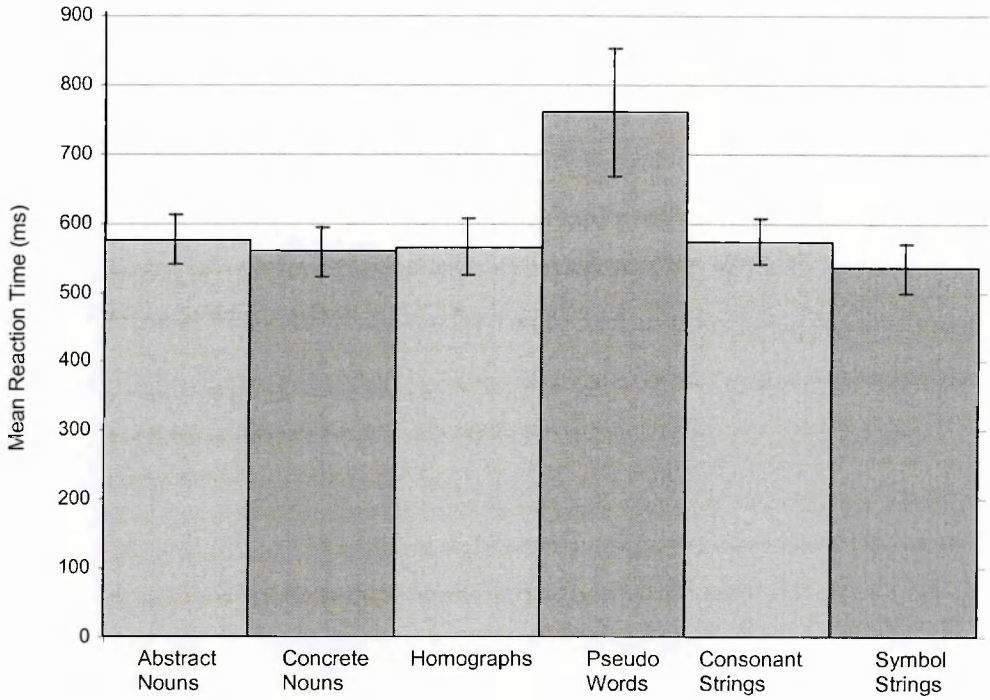


Figure 9.2. The mean reaction time for each of the stimulus categories. The error bars represent the 95% confidence interval for the true population mean calculated from the Standard Errors.

The results of a one-way, repeated measures ANOVA revealed that there was a significant effect of stimulus category on reaction time score ($F_{(1.44, 33.17)} = 28.50$; $p<0.001$). Posthoc comparisons using multiple T tests, corrected for multiple comparisons using the Bonferonni correction, revealed there were significant differences between the pseudoword condition and each of the other stimulus types, and also between the consonant string and the symbol string conditions.

9.5. Behavioural Study: Conclusion

These results are consistent with reports of longer reaction times associated with the processing of nonwords compared to words, for example within a word identification task (Madden et. al. 1996). The reaction times are consistent with the simple model of lexical decision outlined in figure 9.3. Although this model considers lexical decision as a purely serial process, it provides a framework with which to interpret the MEG data. This framework is also in line with an approach that has been adopted within neuroimaging studies (for example, Specht et. al. 2003) which considers the lexical decision of nonwords to be mainly based upon a phonological discrimination process, and the lexical decision of pseudowords to mainly involve a lexical/semantic discrimination process.

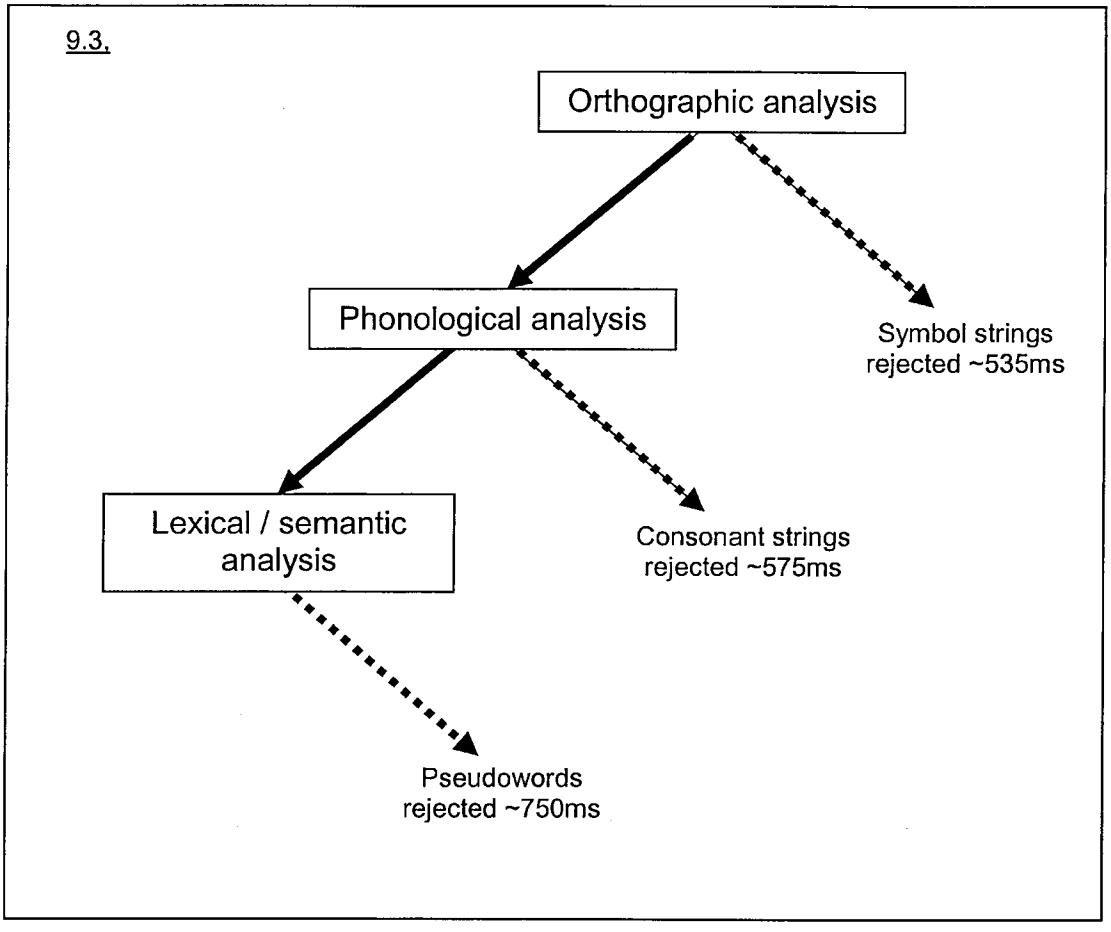


Figure 9.3, A simple model of lexical decision derived from the reaction time data which is also consistent with the approach taken within various lexical decision neuroimaging studies (for example, Specht et. al. 2003). This model provides a framework within which to interpret the results obtained from the MEG study.

9.6, MEG Study: Method

9.6.1, Participants

Ten participants gave informed consent to participate in this study (6 females, 4 males). Participants were either postgraduate students or university lecturers, with English as their native language. All of the participants were right-handed and had normal, or corrected-to-normal vision. Each participant had previously had an anatomical MR volume scan.

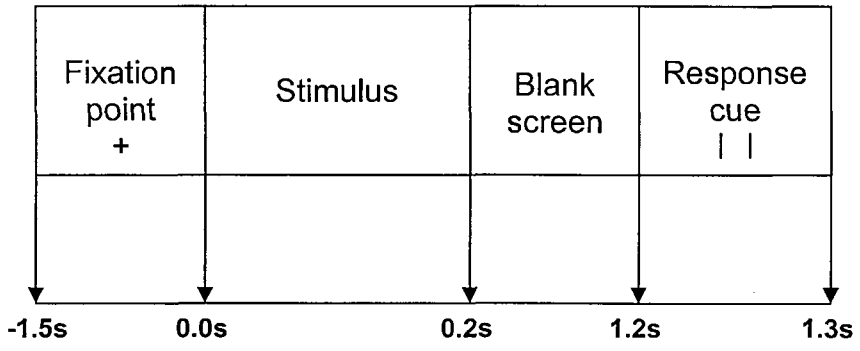
9.6.2, Stimuli

The stimuli consisted of 180 images; 30 abstract nouns, 30 concrete nouns, and 30 homographs, 30 pseudowords, 30 consonant-strings, and 30 symbol-strings. These words and nonwords were taken from the stimulus set used within the behavioural study. Stimulus presentation was identical to that used within the behavioural study.

9.6.3, Procedure

Participants viewed a computer monitor directly through a window in the shielded room. As with the behavioural study, the screen initially displayed a red fixation point in the centre. Following this the words and nonwords were presented in pseudo-random order, in the centre of the screen. Unlike the behavioural study, each string was displayed for 200ms, and then the screen was blank for 1s, at which point two vertical bars were presented at either side of the centre of the screen for 100ms (figure 9.4). Participants were asked to decide whether each string was a word or a nonword and indicate their response when the response cue (vertical bars) appeared. Responses were made via movement of the left index finger. The response was required in order to ensure that participants were carrying out the appropriate task, and the cue was included in an attempt to keep motor activity temporally separate from word processing. The left hand was placed on the armrest with the index finger strapped to a Perspex frame so that a finger movement interrupted a laser beam. Participants were asked to indicate whether they had seen a real word or a nonword, and to move their finger twice in response to a word stimulus, and once in response to a nonword stimulus. MEG data was collected using a 151 channel CTF Omega system.

Figure 9.4. The stimulus sequence



9.6.4, MEG recording and coregistration with MRI data

MEG data was collected using a 151-channel CTF Omega system (CTF Systems Inc., Port Coquitlam, Canada). The data was collected at a sampling rate of 625Hz. Following data acquisition the shape of the participants head was digitised using a 3-D digitiser (Polhemus Isotrack). This surface was matched to that extracted from the participant's anatomical MRI, using Align (www.ece.drexel.edu/ICVC/Align/align11.html) so that the MEG data obtained from each participant was coregistered with their anatomical MRI scan.

9.6.5, Data Analysis

Epochs containing eye blink artefacts were identified by visual inspection, and omitted from further analysis. As the literature (mainly consisting of fMRI and PET studies) failed to provide consistent reports of time windows of interest, SAM analysis was performed using overlapping 200ms time windows in order to span the 800ms following onset of the stimulus (i.e. 0-200ms, 100-300ms, 200-400ms, 300-500ms, 400-600ms, 500-700ms and 600-800ms). Using these time windows, comparisons were made between the different stimulus conditions, and between each stimulus condition and a pre-stimulus 200ms baseline. As the primary aim of the study was to investigate differences associated with the "word like" nature of the stimulus (i.e. between the different non-word conditions), differences between the word conditions are not reported. For each of these comparisons, and for each participant, a 3D statistical parametric map was produced for each of the frequency bands (8-13Hz, 14-20Hz, 20-30Hz, 30-40Hz and 40-50Hz). These images were averaged using Group SAM and the statistical significance of differential effects assessed using SnPM (as described in Chapter 2).

9.7, MEG Study: Results

Using SnPM, voxels were identified in which significant effects were observed within each of the six task conditions relative to their prestimulus baseline. The co-ordinates for each of these voxels are presented within Table 9.1. These main effects are summarised within figure 9.5, together with the mean reaction time for each condition determined by the behavioural study.

9.7.1, Symbol Strings

Within the behavioural study the shortest mean reaction time was associated with the symbol string condition (535ms, SD=88ms). SnPM analysis comparing this condition with the prestimulus baseline identified statistically significant ($p<0.05$) effects within the occipital lobe, and the precuneus (as outlined within Table 9.1). There were no significant effects within regions other than those typically classed as "visual areas".

9.7.2, Word conditions

The three word conditions (those involving the presentation of abstract nouns, concrete nouns, and homographs), were associated with slightly longer reaction times. SnPM results for the comparisons between each of the word conditions and the prestimulus baseline identified a number of significant effects within a range of temporal, frontal and cerebellar regions. As can be seen from Table 9.1, differences between the different word types can be inferred from the different effects observed within each word type condition with respect to the prestimulus baseline, although such differences are beyond the scope of this thesis.

9.7.3, Pseudo words

The stimulus condition associated with the longest mean reaction time within the behavioural study was the pseudoword condition (760ms, SD=224ms). SnPM results revealed that there were three voxels in which statistically significant ($p<0.05$) effects were observed in response to the presentation of pseudowords, relative to the prestimulus interval (figure 9.6).

Table 9.1,

The co-ordinates for each of the voxels in which significant effects ($p<0.05$) were identified within each of the six stimulus conditions relative to their prestimulus baseline, using SnPM analysis. Italics denote the effects associated with ERS within the stimulus condition compared to the prestimulus baseline, the others relate to ERD within the stimulus condition.

	Abstract Nouns	**Concrete Nouns**	**Homographs**	**Pseudo Words**	**Consonant Strings**	**Symbol Strings**
0-200ms						
8-20Hz		Right occipital cuneus 18, -87, 27		*Right cerebellum* *24, -99, -42*		
20-30Hz						
30-40Hz						
40-50Hz	*Right cerebellum* *3, -54, -27*					
100-300ms						
8-20Hz		Right occipital cuneus BA19 9, –99, 30				
20-30Hz						
30-40Hz						
40-50Hz	Left middle frontal gyrus -36, 51, 21					
200-400ms						
8-20Hz						

20-30Hz						
30-40Hz						Left parietal, precuneus -21, -63, 33
40-50Hz						
300-500ms						
8-20Hz	Right parietal lobe BA9 33, -84, 39		Left middle frontal gyrus BA10 -51, 60, -6 Right inferior temporal gyrus BA20 *45, -15, -42*			Right inferior occipital gyrus 33, -93, -12
20-30Hz	Right parietal BA19 15, -93, 42	Left cerebellum -15, -87, -39	Left cerebellum -45, -87, -33		Right cerebellum 60, -75, -33	
30-40Hz					*Left middle occipital gyrus BA37 -63, -75, -15*	
40-50Hz						
400-600ms						
8-20Hz					Right occipital lobe, cuneus 12, -93, 39	
20-30Hz						
30-40Hz						
40-50Hz				Right inferior parietal BA40 54, -42, 69		
500-						

700ms						
8-20Hz	Left superior temporal gyrus -60, -21, 6		*Left parahippocampal gyrus – Amygdala* *-30, -3, -18*			
20-30Hz	*Right inferior occipital gyrus BA18* *39, -93, -9*					
30-40Hz	*Right cerebellum* *27, -96, -45*				Left middle occipital gyrus -63, -75, -15	*Right middle occipital gyrus* *33, -102, 3*
40-50Hz				Left middle frontal gyrus BA46 -48, 57, 12	Left superior temporal gyrus -36, -39, 9	
600-800ms						
8-20Hz						
20-30Hz					Right parietal postcentral gyrus 42, -27, 54	
30-40Hz			Next to right middle frontal gyrus 45, 3, 72			
40-50Hz						

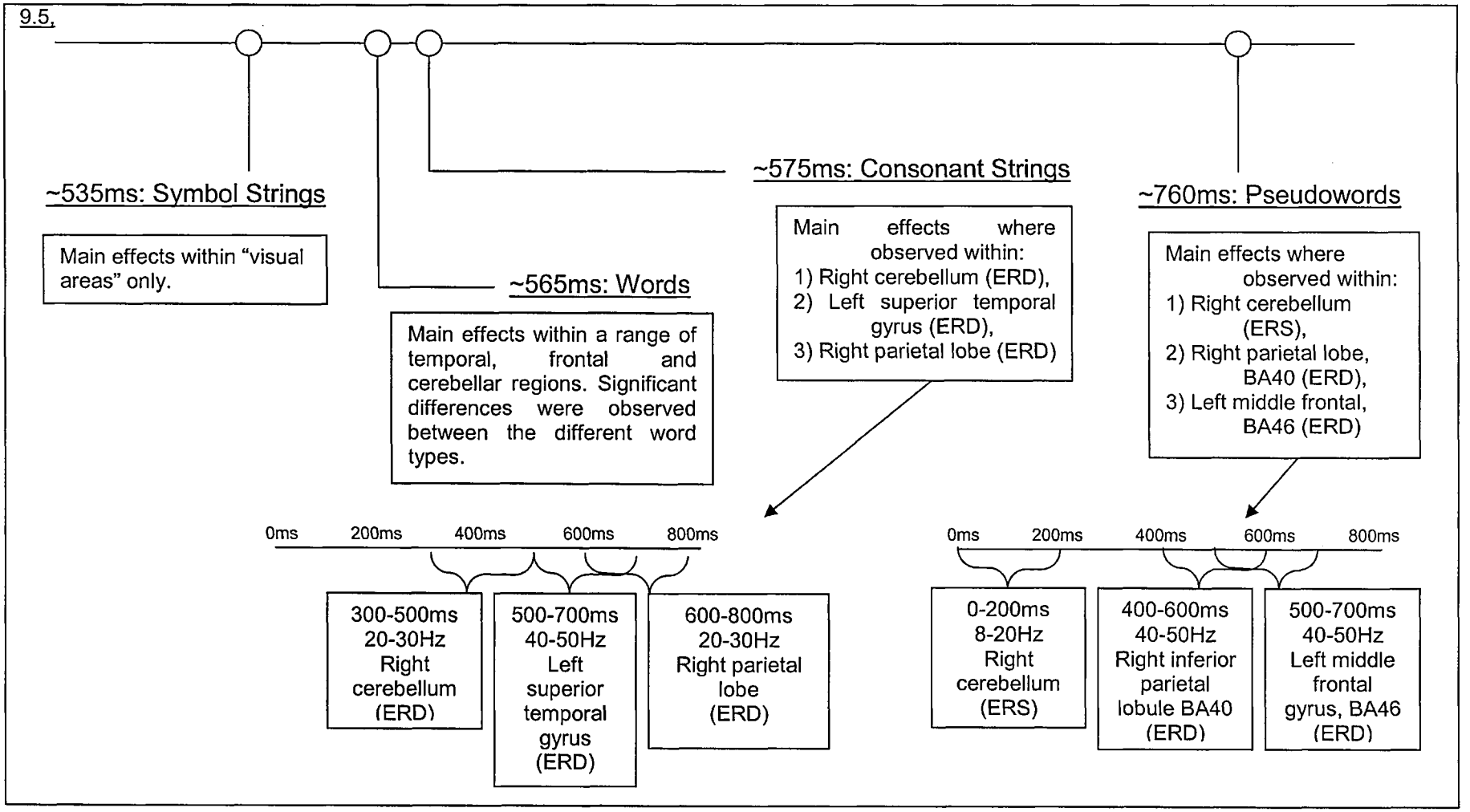


Figure 9.5, A summary of the main effects associated with each of the stimulus conditions compared to their prestimulus baseline, as identified using SnPM analysis. The mean reaction times for each condition, as determined by the behavioural study, are also shown.

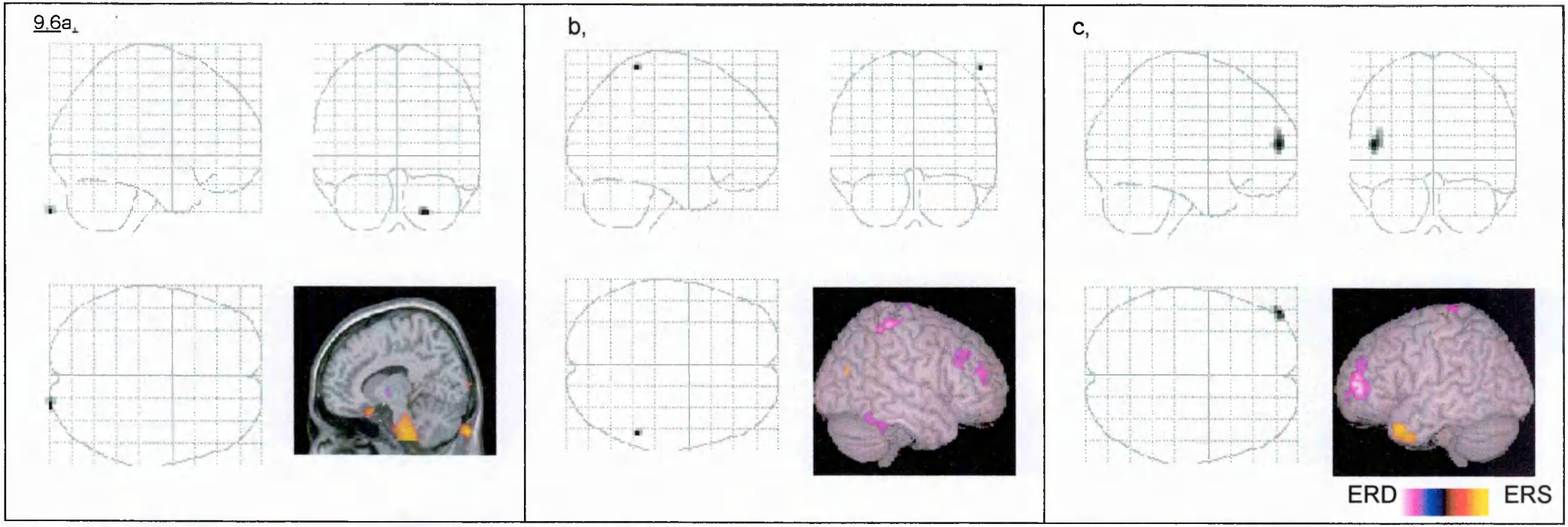


Figure 9.6. Glass brain SnPM results showing statistically significant ($p<0.05$) differential effects between the condition involving the presentation of pseudowords and the prestimulus baseline within:

a) a right cerebellar voxel (talairach co-ordinates 24, -99 –42), where the pseudoword condition is associated with ERS within the 0-200ms time window and the 8-20Hz frequency band (the Group SAM rfx image shows that at this voxel t=5.90),

b) a right parietal voxel (talairach co-ordinates 54, -42, 69), where the pseudoword condition is associated with ERD within the 400-600ms time window, and the 40-50Hz frequency band (the Group SAM rfx image shows that at this voxel t=-5.68),

c) a left middle frontal (BA46) voxel (talairach co-ordinates –48, 57, 12), where the pseudoword condition is associated with ERD within the 500-700ms time window, and the 40-50Hz frequency band (the Group SAM rfx image shows that at this voxel t=-7.01). For each of these comparisons Group SAM rfx images show values corresponding to $-3>t>3$).

Firstly, within the first 200ms of stimulus onset, and within the 8-20Hz frequency band, a significant power increase (ERS) was identified at a right cerebellar voxel. Although the individual normalised SAM images for this comparison showed no peak values of t>2 within this region, the voxel in which the significant group-level effect was observed was associated with ERD for all but one of the participants.

For each participant, a virtual electrode was placed at co-ordinates corresponding to those at which the significant group-level effect was identified using SnPM, and Mann Whitney time-frequency representations were produced. An example time-frequency representation for one participant is displayed in figure 9.7, and shows that for this participant peak values of the Mann Whitney Z statistic (Z~3.5) corresponding to ERS within the pseudoword condition were observed within a frequency band of 4-6Hz, within the first 50ms of stimulus onset. This seemed to be a relatively consistent effect, with 6 participants showing peak values of the Mann Whitney Z statistic (Z>2) within frequency bands ranging from 3 to 6Hz. In each of these cases the effect was observed early in the epoch (with peak Mann Whitney Z values occurring within the first 200ms of stimulus onset, in line with the SnPM results).

Secondly, significant ERD was observed within the right parietal lobule, BA40, between 400 and 600ms post stimulus onset, within the 40-50Hz frequency band. Again, although individual normalised SAM images for this pseudoword versus prestimulus comparison showed no peak values of t>2 within this region, all but one of the participants showed ERD within the voxel identified within SnPM as showing significant group-level differential effects.

For each participant, a virtual electrode was placed at co-ordinates corresponding to those at which the significant group-level effect was identified using SnPM, and Mann Whitney time-frequency representations were produced. An example representation for one participant is displayed in figure 9.8, and shows that for this participant a peak Mann Whitney Z statistic (Z>2) corresponding to ERD within the pseudoword condition, was observed within a 43-45Hz frequency band at approximately 460ms following stimulus onset. Again this seemed to be a relatively consistent effect, with 6 participants, showing peak values of the Mann Whitney Z statistic (Z>2) within a 42-44Hz frequency, although the latencies at which these peaks were observed ranged from 250ms to 800ms.

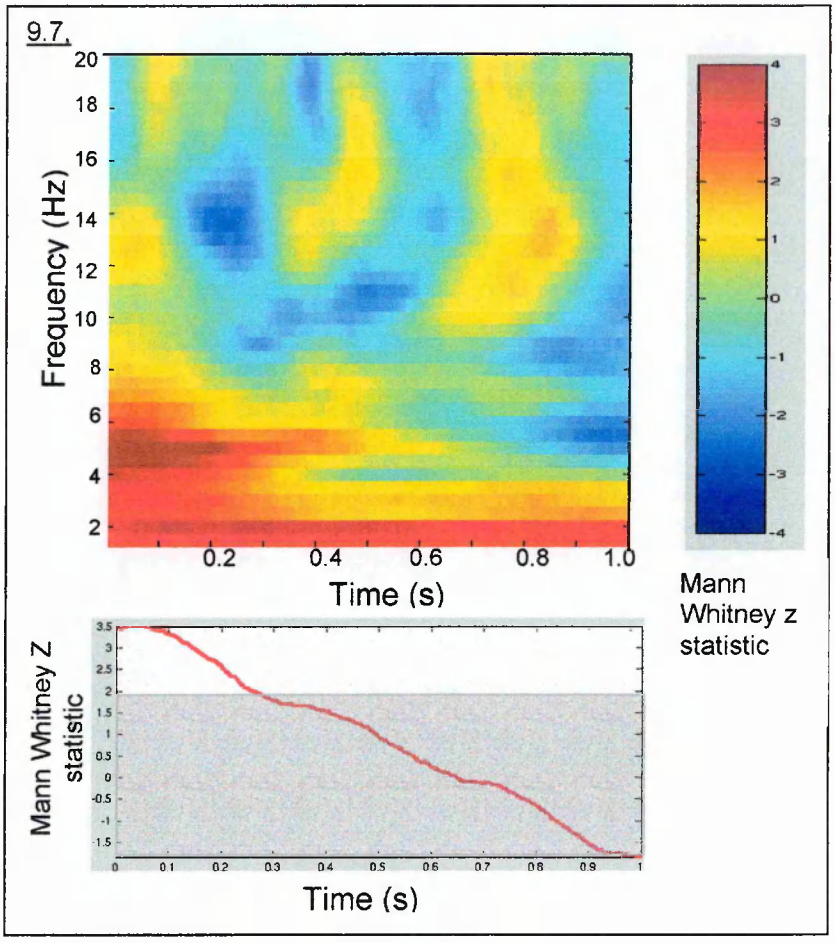


Figure 9.7. An example time-frequency Mann Whitney representation for the pseudoword condition compared to the prestimulus baseline for a virtual electrode placed within the right cerebellum of one participant, at co-ordinates corresponding to those at which significant group-level ERS was identified within the pseudoword condition (0-200ms, 8-20Hz), using SnPM. The colour represents the Mann Whitney z statistic. The line graph shows the Mann Whitney z statistic as a function of time for the 4Hz to 6Hz frequency band. In the case of this participant, $Z>2$ (corresponding to $p<0.05$) until approximately 280ms following stimulus onset.

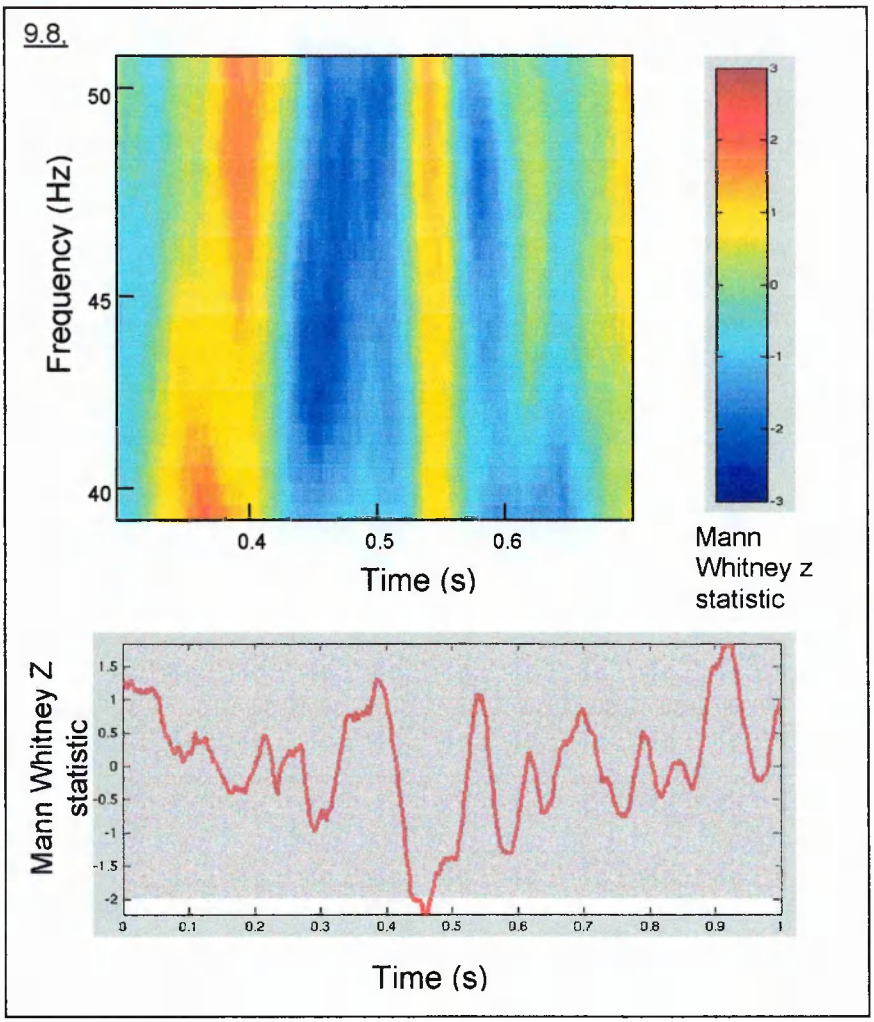


Figure 9.8, An example time-frequency Mann Whitney representation for the pseudoword condition compared to the prestimulus baseline for a virtual electrode placed within the right parietal lobule (BA40) of one participant, at co-ordinates corresponding to those at which significant group-level ERD was identified within the pseudoword condition (400-600ms, 40-50Hz), using SnPM. The colour represents the Mann Whitney z statistic. The line graph shows the Mann Whitney z statistic as a function of time for the 43Hz to 45Hz frequency band. For this participant Z<-2 (corresponding to $p<0.05$) at approximately 460ms following stimulus onset.

Also within the 40-50Hz frequency band, but between 500 and 700ms following stimulus onset, a significant power decrease (ERD) was identified within a left middle frontal (BA46) voxel. The individual normalised SAM images for the 500-700ms, 40-50Hz, pseudoword versus prestimulus comparisons revealed that although for all participants ERD was observed within the left middle frontal voxel identified using SnPM analysis, no peak values of t>2 were observed within this region.

For each participant, a virtual electrode was placed at co-ordinates corresponding to those at which the significant group-level effect had been identified using SnPM, and Mann Whitney time-frequency representations were produced. An example time-frequency representation for one participant is displayed in figure 9.9, and shows that for this participant a peak value of the Mann Whitney Z statistic of ~-2.5 corresponding to ERD within the pseudoword condition was observed at approximately 500ms following stimulus onset. Although there seemed to be a relatively high degree of temporal variability, eight of the participants showed ERD within the pseudo word condition, corresponding to Z>2, at frequencies ranging from 40-48Hz, and within a 300 to 900ms range.

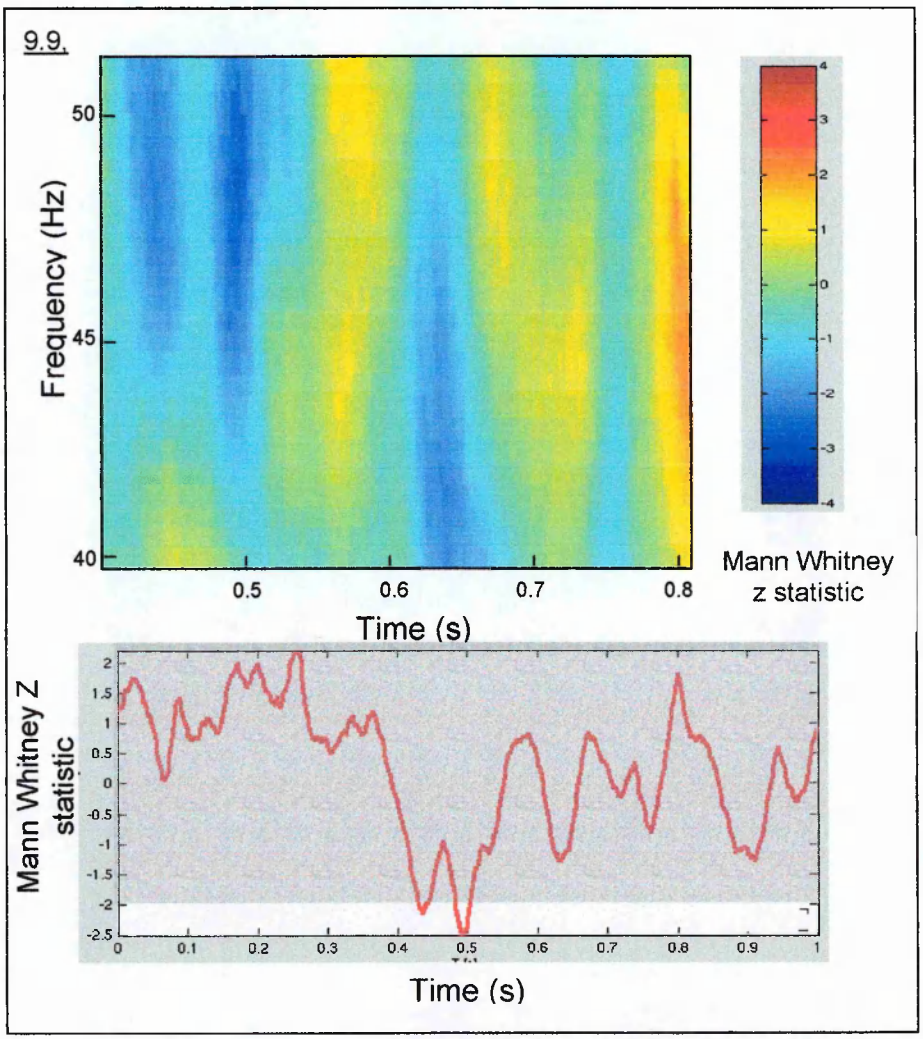


Figure 9.9. An example time-frequency Mann Whitney representation for the pseudoword condition compared to the prestimulus baseline for a virtual electrode placed within the left middle frontal region (BA46) of one participant, at co-ordinates corresponding to those at which significant group-level ERD was identified within the pseudoword condition (500-700ms, 40-50Hz), using SnPM. The colour represents the Mann Whitney z statistic. The line graph shows the Mann Whitney z statistic as a function of time for the 47Hz to 49Hz frequency band. For this participant Z~-2.5 (corresponding to $p<0.05$) at approximately 500ms following stimulus onset.

Similarly, left frontal effects were also observed within both the abstract noun condition (100-300ms, 40-50Hz) and the homograph condition (300-500ms, 8-20Hz) compared to their prestimulus baselines (figure 9.10). However, unlike the nonword conditions, these word conditions were associated with a power increase indicative of ERS.

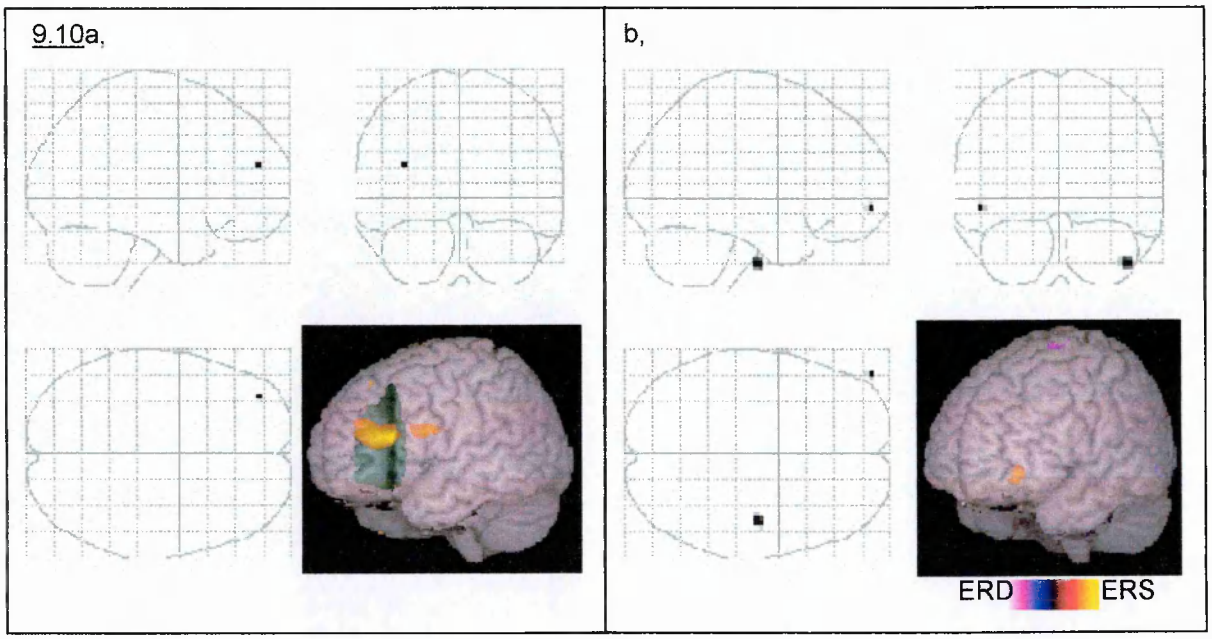


Figure 9.10, Glass brain SnPM results showing statistically significant ($p<0.05$) effects associated with

a) the abstract noun condition relative to the prestimulus baseline within a left middle frontal voxel (talairach co-ordinates –36, 51, 21), for the 100-300ms, 40-50Hz comparison, the Group SAM rfx image shows that this voxel is associated with ERS within the abstract noun condition ($t= 7.01$), and

b) the homograph condition relative to prestimulus baseline within a left middle frontal (BA10) voxel (talairach co-ordinates –51, 60, -6), for the 300-500ms, 8-20Hz comparison. The Group SAM rfx image shows that this voxel is associated with ERS within the homograph condition ($t=6.34$). The Group SAM rfx images show values corresponding to $-3>t>3$).

9.7.4, Consonant Strings

SnPM results for the comparison between the condition involving the presentation of consonant strings and the prestimulus baseline also revealed statistically significant effects ($p<0.05$) within three voxels (figure 9.11).

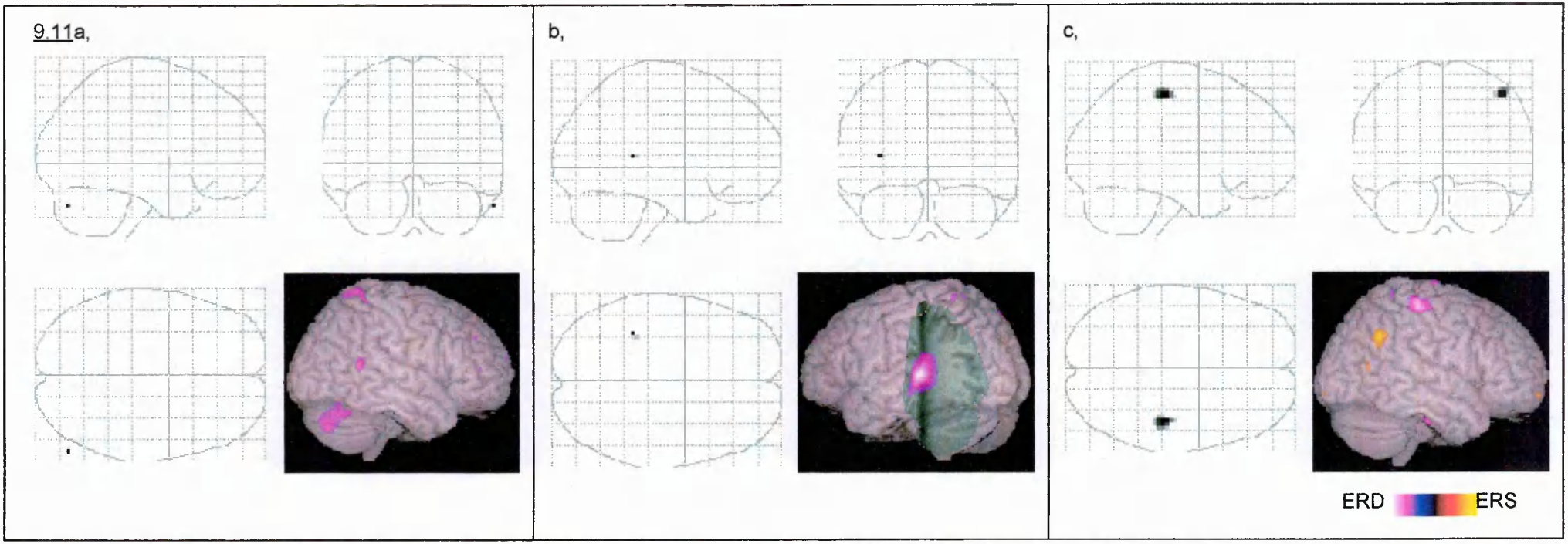


Figure 9.11, Glass brain SnPM results showing statistically significant ($p<0.05$) differential effects between the condition involving the presentation of consonant strings and prestimulus time within

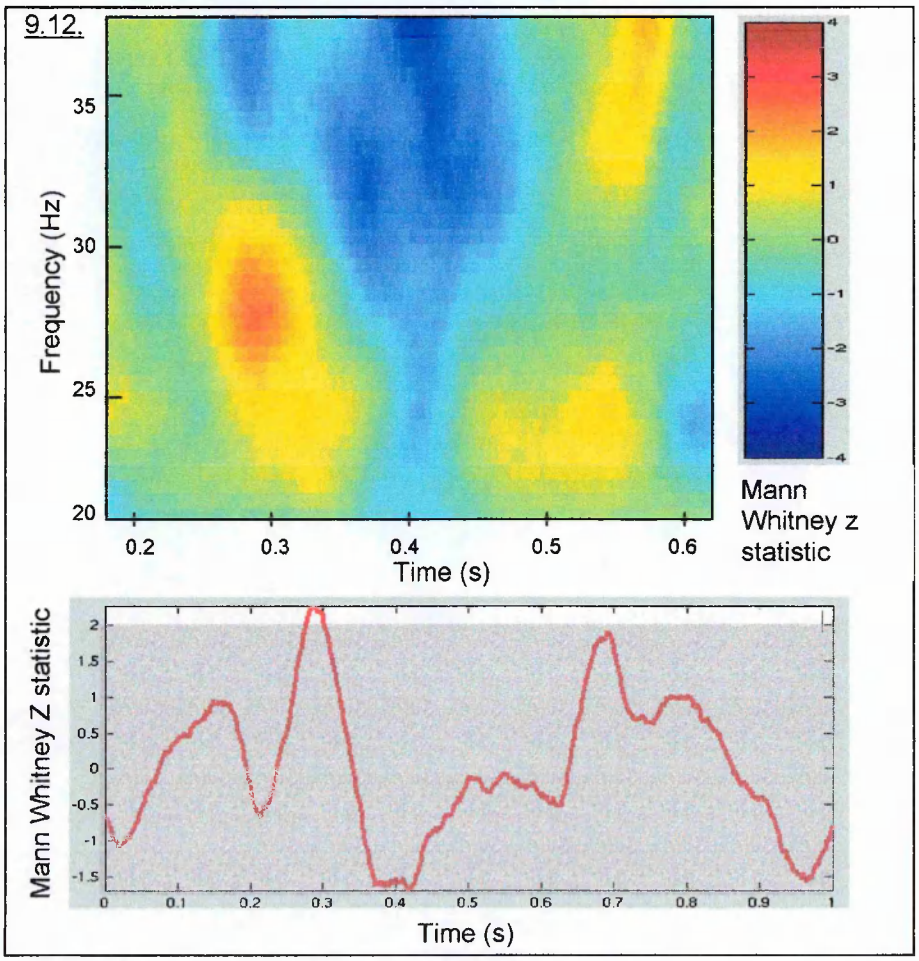
a) the right cerebellar voxel (talairach co-ordinates 60, -75, -33), where the consonant string condition is associated with ERD within the 300-500ms time window and the 20-30Hz frequency band (the Group SAM rfx image shows that at this voxel t= -4.7),

b) a left superior temporal voxel (talairach co-ordinates –36, -39, 9), where the consonant string condition is associated with ERD within the 500-700ms time window, and the 40-50Hz frequency band (the Group SAM rfx image shows that at this voxel t= -6.02),

c) a right parietal voxel (talairach co-ordinates 42, -27, 54), where the pseudoword condition is associated with ERD within the 600-800ms time window, and the 20-30Hz frequency band (the Group SAM rfx image shows that at this voxel t=-6.04). For each of these comparisons Group SAM rfx images show values corresponding to –3>t>3).

As with the pseudoword condition, the first effect was observed within the right cerebellum, however, in the case of the consonant string condition this region was associated with ERD, and the effect occurred later (300-500ms, 20-30Hz).

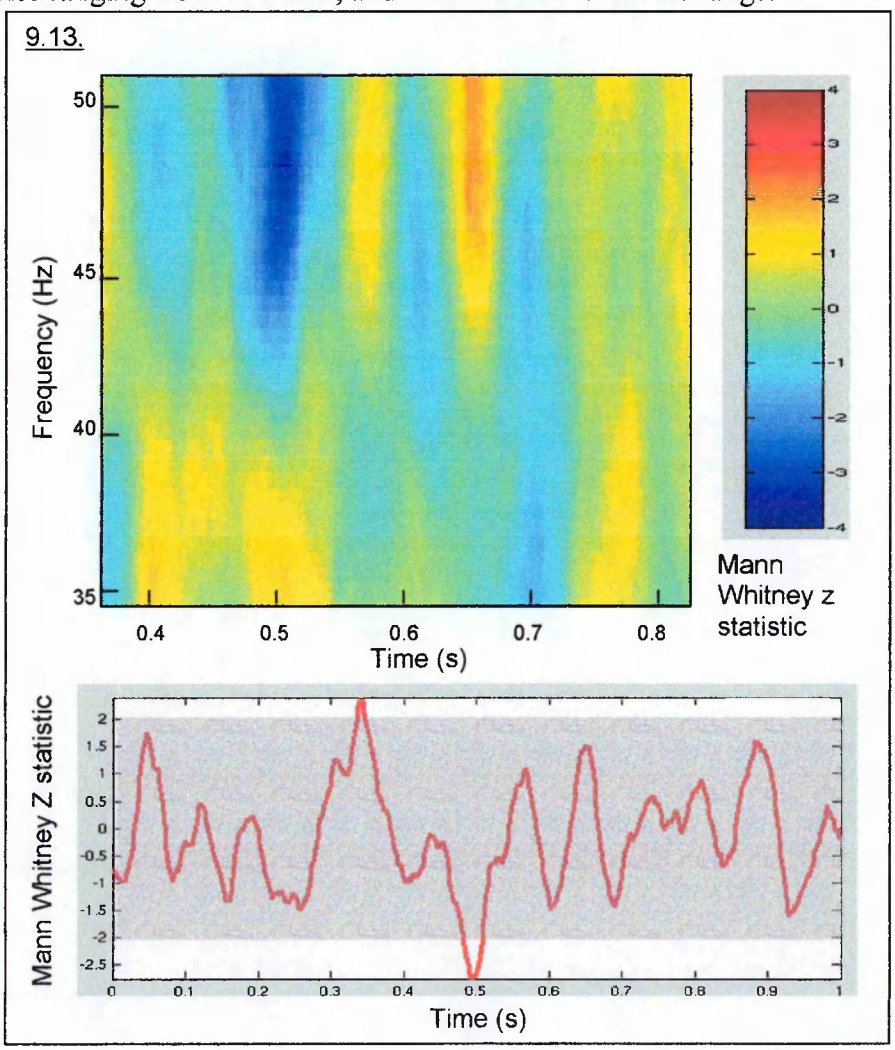
For each participant, a virtual electrode was placed at co-ordinates corresponding to those at which the significant group-level effect was identified using SnPM, and Mann Whitney time-frequency representations were produced. An example representation for one participant is displayed in figure 9.12, and shows that for this participant a peak value of the Mann Whitney Z statistic (Z>2), corresponding to ERS within the pseudoword condition, was observed at approximately 300ms. Although again there seemed to be a relatively high degree of temporal variability, five of the participants showed peak Z values (Z>2), corresponding to ERS within the pseudo word condition, at frequencies ranging from 23-26Hz, and within a 300 to 800ms range.



ure 9.12. An example time-frequency Mann Whitney representation for the consonant string condition npared to the prestimulus baseline for a virtual electrode placed within the right cerebellum of one ticipant, at co-ordinates corresponding to those at which significant group-level ERS was identified hin the consonant string condition (300-500ms, 20-30Hz), using SnPM. The colour represents the nn Whitney z statistic. The line graph shows the Mann Whitney z statistic as a function of time for the Hz to 27Hz frequency band. For this participant Z>2 (corresponding to p<0.05) at approximately)ms following stimulus onset.

The second significant effect was ERD within the left superior temporal gyrus. This was observed within the 500-700ms time window, and the 40-50Hz frequency band.

For each participant, a virtual electrode was placed at co-ordinates corresponding to those at which the significant group-level effect had been identified using SnPM, and Mann Whitney time-frequency representations were produced. An example representation for one participant is displayed in figure 9.13, and shows that for this participant a peak value of the Mann Whitney Z statistic (Z~-2.5) corresponding to ERD within the consonant string condition was observed at approximately 500ms. Five of the participants showed peak Z values (Z>2) corresponding to ERD within the consonant string condition, at frequencies ranging from 41-50Hz, and within a 500 to 600ms range.



ɪure 9.13. An example time-frequency Mann Whitney representation for the consonant string ıdition compared to the prestimulus baseline for a virtual electrode placed within the left superior ıporal gyrus of one participant, at co-ordinates corresponding to those at which significant group-el ERD was identified within the consonant string condition (500-700ms, 40-50Hz), using SnPM. e colour represents the Mann Whitney z statistic. The line graph shows the Mann Whitney Z tistic as a function of time for the 49Hz to 51Hz frequency band. For this participant Z~-2.7 ırresponding to p<0.05) at approximately 500ms following stimulus onset.

As with the pseudoword condition, a right parietal voxel, in the region of BA40, was associated with statistically significant ERD within the consonant string condition. This effect occurred later than the effect observed within the pseudoword condition (600-800ms, 20-30Hz). No significant effects were observed within this region for any of the word conditions (i.e. those involving the presentation of abstract nouns, concrete nouns, or homographs).

For each participant, a virtual electrode was placed at co-ordinates corresponding to those at which the significant group-level effect was identified using SnPM, and Mann Whitney time-frequency representations were produced. An example representation for one participant is displayed in figure 9.14, and shows that for this participant a peak value of the Mann Whitney Z statistic ($Z\sim-4.0$) corresponding to ERD within the consonant string condition was observed at approximately 660ms following stimulus onset. Seven of the participants showed such ERD peaks (corresponding to $Z<-2$) within the consonant string condition, at frequencies ranging from 22 to 28Hz, and within a 500 to 850ms range.

9.7.5. Pseudowords compared to consonant strings

By directly comparing the pseudoword and consonant string conditions, significant differential effects were observed within the left middle temporal gyrus (0-200ms, 20-30Hz) and the left inferior parietal lobule, BA40 (200-400ms, 8-20Hz) (figure 9.15).

The first was within a left middle temporal voxel (0-200ms, 20-30Hz). For each participant, a virtual electrode was placed at co-ordinates corresponding to those at which the significant group-level differential effect was identified using SnPM, and Mann Whitney time-frequency representations were produced for both the conditions compared to their prestimulus baseline. Example representations for one participant are displayed in figure 9.16, and show that for this participant the consonant string condition is associated with a peak value of the Mann Whitney Z statistic ($Z\sim-2.7$) corresponding to ERD within the 19-21Hz frequency band, within the first 100ms following stimulus onset. No such peaks were observed within the pseudoword condition. Five of the participants showed such ERD peaks ($Z<-2$) within the consonant string condition but not in the pseudoword condition, within the first 100ms of stimulus onset, and within frequency bands ranging from 19Hz to 30Hz.

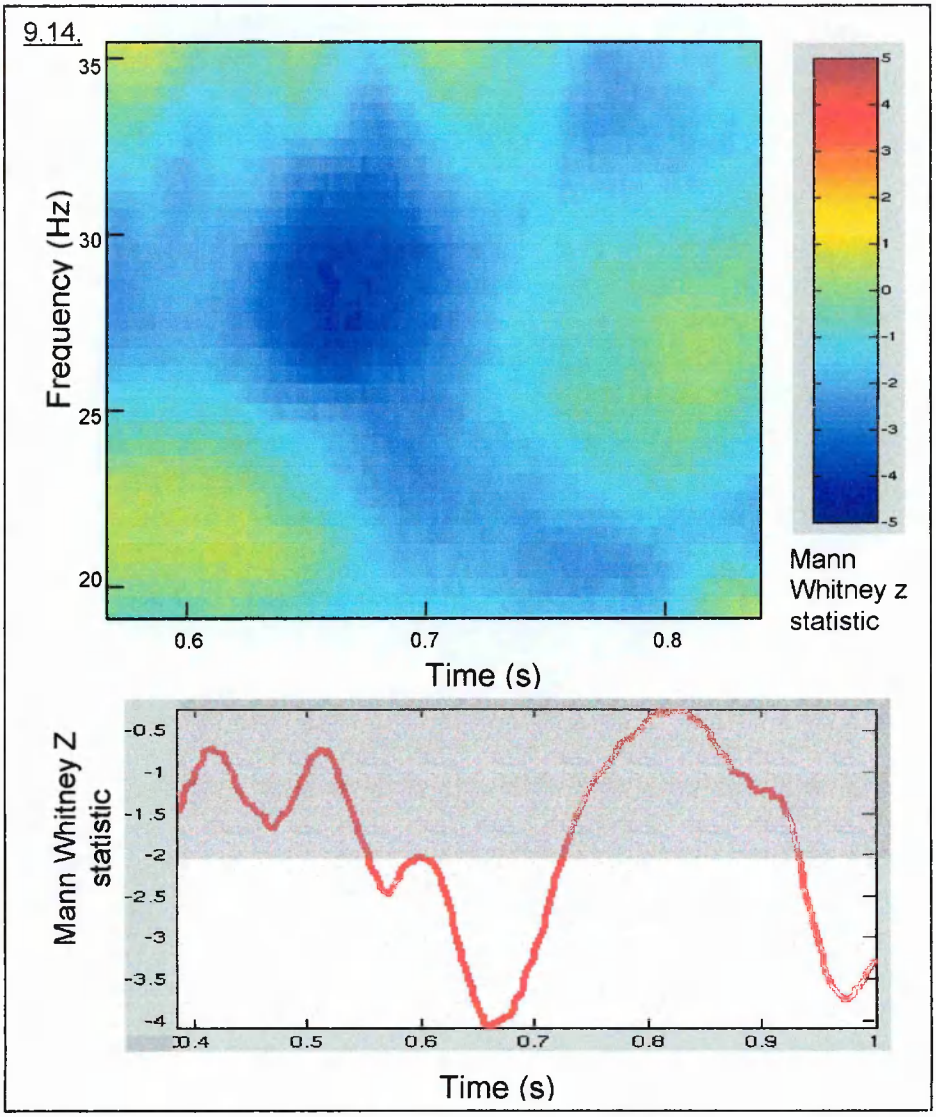


Figure 9.14. An example time-frequency Mann Whitney representation for the consonant string condition compared to the prestimulus baseline for a virtual electrode placed within the right parietal region (BA40) of one participant, at co-ordinates corresponding to those at which significant group-level ERD was identified within the consonant string condition (600-800ms, 20-30Hz), using SnPM. The colour represents the Mann Whitney z statistic. The line graph shows the Mann Whitney z statistic as a function of time for the 27Hz to 29Hz frequency band. For this participant Z~-4.0 (corresponding to $p<0.05$) at approximately 660ms following stimulus onset.

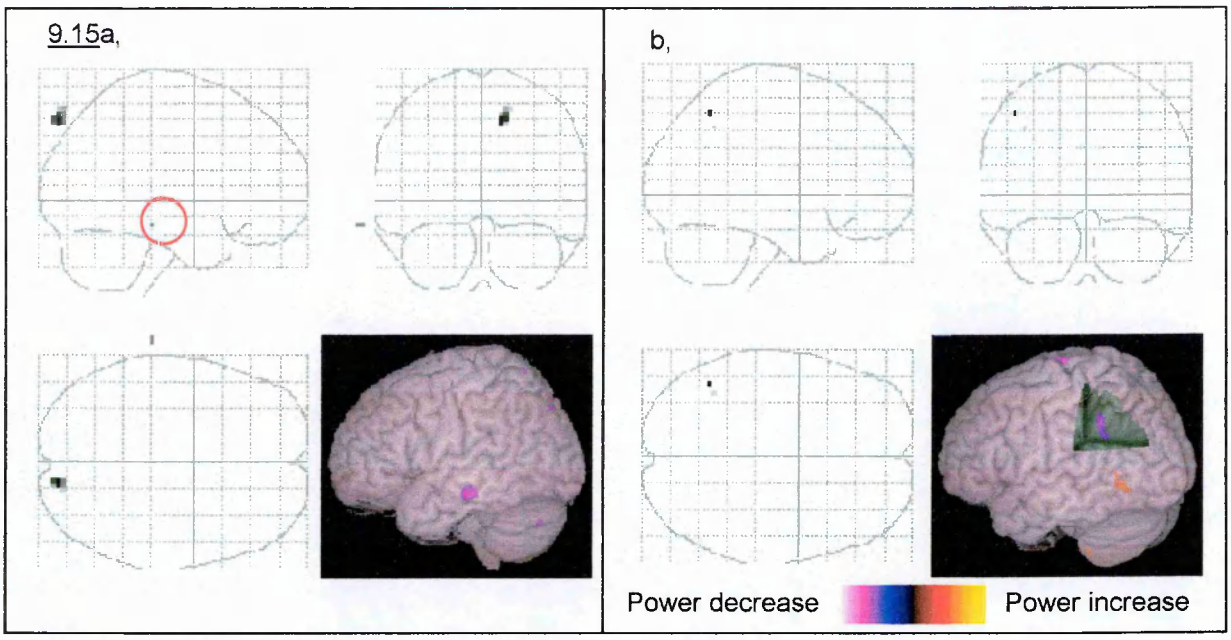


Figure 9.15. Glass brain SnPM results showing statistically significant ($p<0.05$) differential effects between the pseudoword condition and the consonant string condition within

a) a left middle temporal voxel (talairach co-ordinates –75, -27, -15), for the 0-200ms, 20-30Hz comparison. The Group SAM rfx images shows that this voxel is associated with enhanced ERD within the consonant string condition (t= -4.64) compared to the pseudo word condition (t=-0.96), and that the differential effect is associated with a t value of –6.16, and

b) two left inferior parietal voxels in the region of BA40 (talairach co-ordinates –45, -57, 51 and –39, -54, 42), for the 200-400ms, 8-20Hz comparison. Group SAM rfx images show that this voxel is associated with ERD within the pseudoword condition (t=-0.30 and t=-0.06), and ERS within the consonant string condition (t=1.06 and t=0.94). The most significant differential effect is associated with a t value of –4.17. The Group SAM rfx images show differential effects corresponding to –3>t>3).

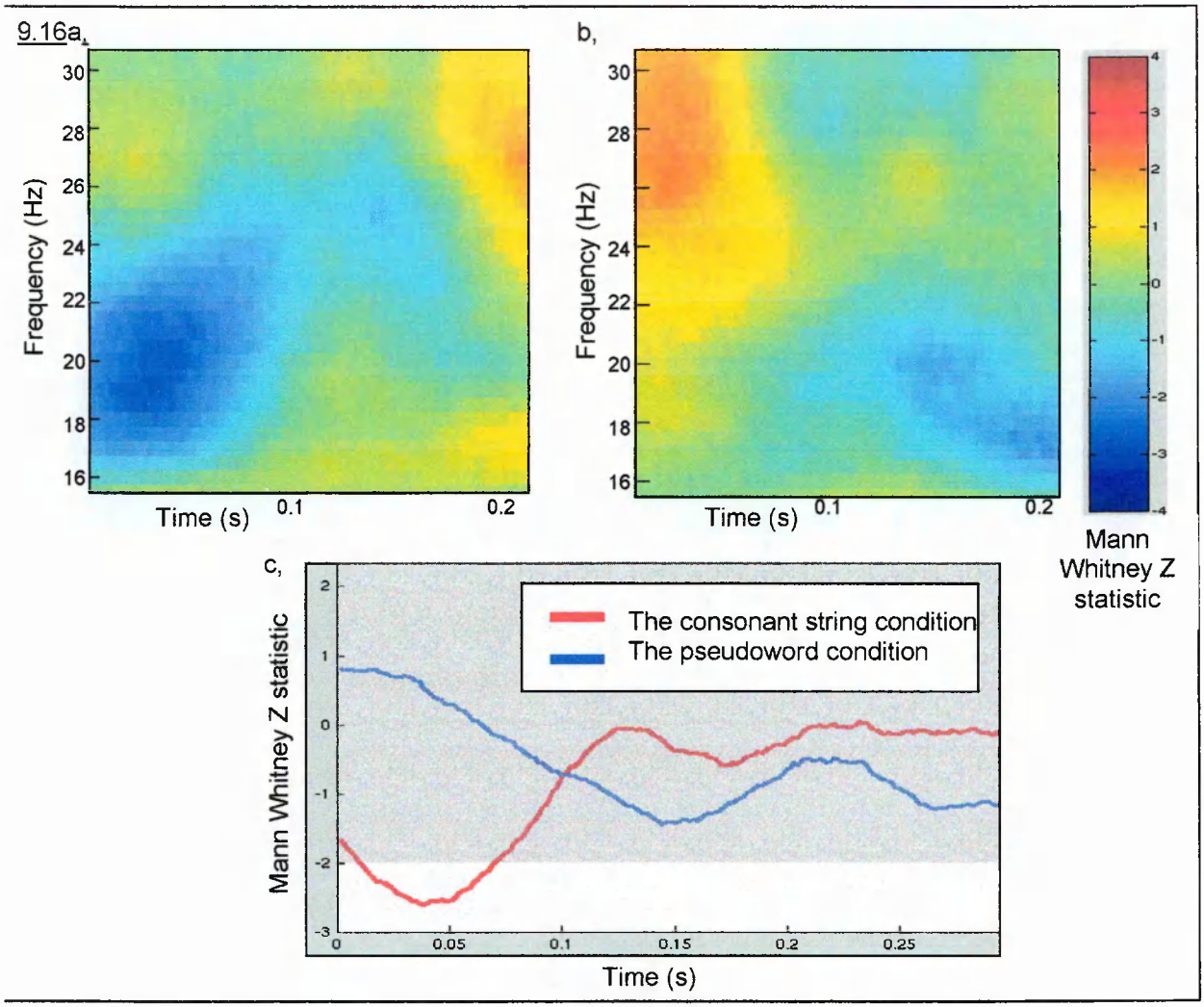


Figure 9.16. Example time-frequency Mann Whitney represenations for

a) the consonant string condition compared to the prestimulus baseline, and

b) the pseudoword condition compared to the prestimulus baseline, for a virtual electrode placed within a left middle temporal voxel for one participant, at co-ordinates corresponding to those at which a significant group-level differential effect was observed using SnPM. The colour represents the Mann Whitney z statistic.

c) The line graph shows the Mann Whitney z statistic as a function of time for the 19Hz to 21Hz frequency band. For this participant, and this frequency band, Z>2 (corresponding to $p<0.05$) within the first 100ms following stimulus onset for the consonant string condition, but not the pseudoword condition.

This temporal effect was similar to the significant temporal effects observed within comparisons between the pseudoword condition and the other stimulus conditions (figure 9.17).

The second significant differential effect between the pseudoword and consonant string conditions was observed within a left inferior parietal voxel (BA40) (200-400ms, 8-20Hz).

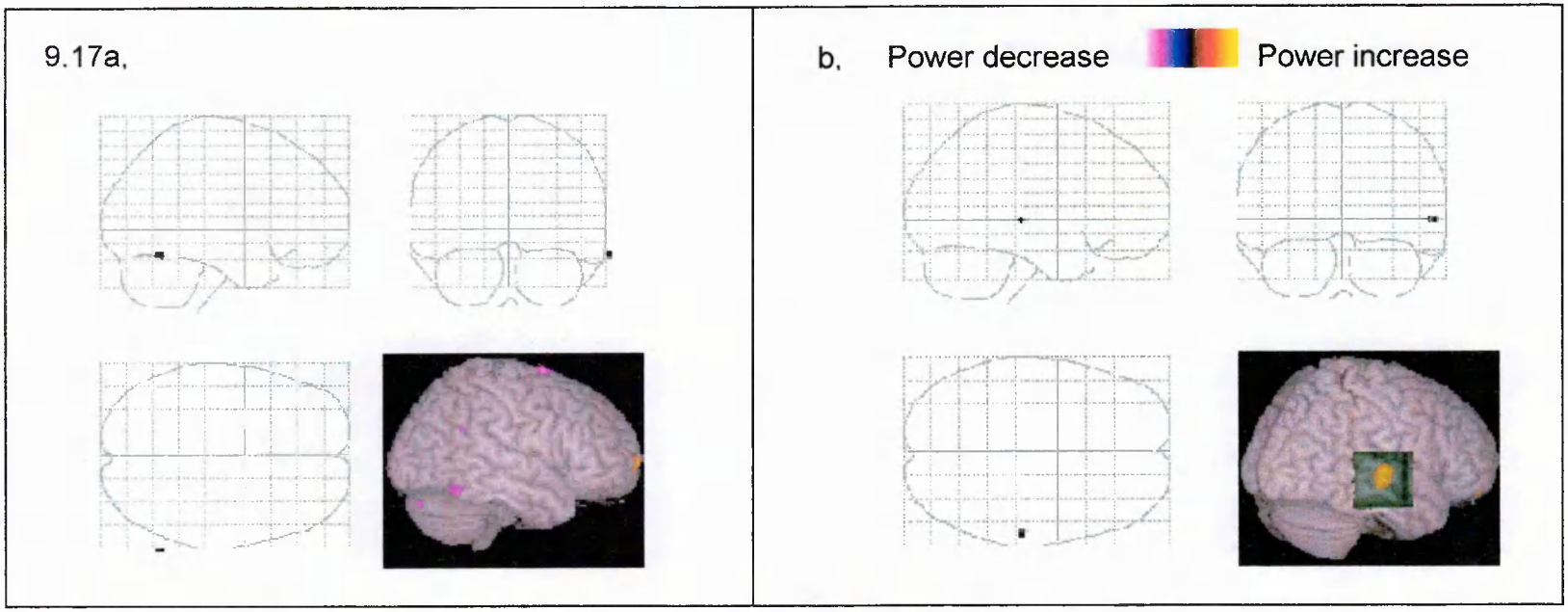
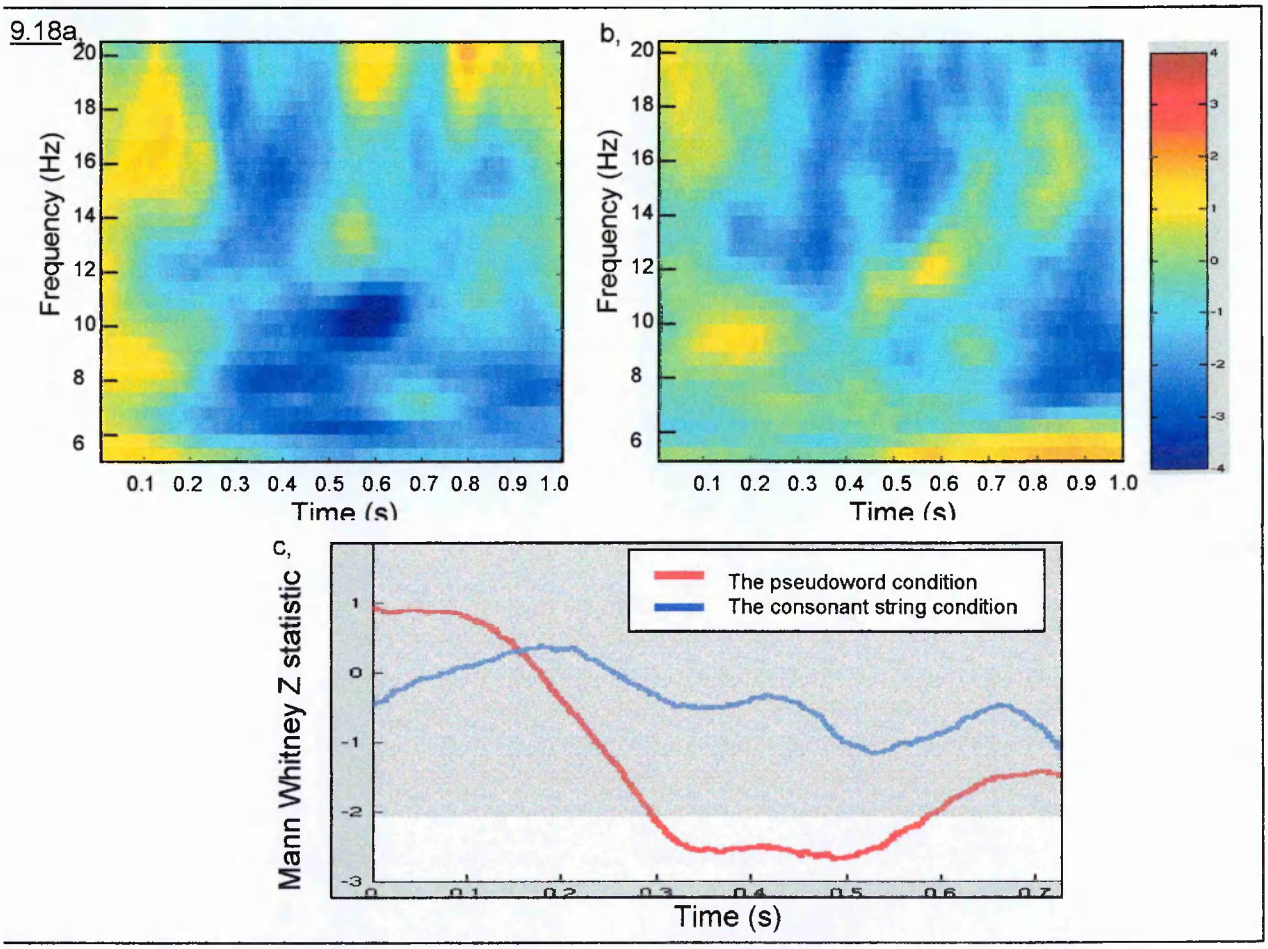


Figure 9.17, Glass brain SnPM results showing statistically significant ($p<0.05$) group-level differential effects

a) between the pseudo word and concrete noun condition within a right inferior temporal voxel (BA20) (talairach co-ordinates 69, -57, -18), within the 300to500ms time window, and the 30-40Hz frequency band. Group SAM rfx images show that this voxel is associated with ERD within the pseudo word condition (t=-1.58), but not within the concrete noun condition (t=0.42). The Group SAM rfx image presented within this figure shows the differential effect (t=-6.64), and

b) between the pseudo word condition and the symbol string condition, within a right superior temporal voxel (talairach co-ordinates 60, -24, 0), within the 200-400ms time window, and 8-20Hz frequency band. Group SAM rfx images show that within the pseudo word condition this voxel is associated with ERS (t=2.25), whereas within the symbol string condition it is associated with ERD (t=-1.88). The Group SAM rfx image presented within this figure shows the differential effect (t= 4.74). All the Group SAM rfx images within this figure show values corresponding to $-3>t>3$).

For each participant, a virtual electrode was placed at co-ordinates corresponding to those at which the significant group-level differential effect was identified using SnPM, and Mann Whitney time-frequency representations were produced for both the conditions compared to their prestimulus baseline. Example representations for one participant are displayed in figure 9.18, and show that for this participant the pseudoword condition is associated with a peak value of the Mann Whitney Z statistic (Z~-2.7) corresponding to ERD within the 7-9Hz frequency band, between 300 and 500ms following stimulus onset. No such peaks were observed within the consonant string condition. Three of the participants showed such ERD peaks (Z<-2) within the pseudoword condition but not in the consonant string condition. These peaks occurred within the 250ms to 500ms range, and within frequency bands between 8Hz and 17Hz.



re 9.18. Example time-frequency Mann Whitney represenations for
: pseudoword condition compared to the prestimulus baseline, and
: consonant string condition compared to the prestimulus baseline for a virtual electrode placed within
inferior parietal voxel (BA40) for one participant, at co-ordinates corresponding to those at which a
ficant group-level differential effect was observed using SnPM. The colour represents the Mann
ney z statistic.
e line graph shows the Mann Whitney z statistic as a function of time for the 7Hz to 9Hz frequency
For this participant, and this frequency band, Z<-2.0 (corresponding to p<0.05) between 300ms and
s following stimulus onset for the pseudoword condition, but not the consonant string condition.

9.8, MEG Study: Conclusions

9.8.1, Symbol strings

Compared to the prestimulus baseline, the presentation of symbol strings resulted in significant ERD/ERS effects within bilateral occipital regions. No other regions were associated with significant differential effects for this comparison, and no other stimulus condition showed differential effects that were confined to occipital regions. The results of the lexical decision behavioural study also identified the symbol string condition as being associated with the shortest mean reaction time. Both of these results are consistent with the interpretation that within the symbol string condition processing did not proceed beyond low level visual analysis.

Although slightly later, the occipital responses reported within the symbol string condition seem to be functionally consistent with the 90ms occipital evoked response linked to low level visual analysis by Schendan et. al. (1998), and the right occipital "type one activation" reported by Tarkianen et. al. (1999), which they describe as reflecting "the kind of low level processing that is common to all visual stimuli, such as the extraction of oriented contrast borders" (page 2128). Xiang, Wilson, Otsubo, Ishii & Chuang (2001) also used SAM analysis, and reported changes within occipital/parietal cortices that were very similar during the presentation of word and symbol strings, despite the long time window analysed (1800ms). The authors conclude that these areas are related to "spatiovisual information processing" (Xiang et. al. 2001, page 3926) which occurs within both word and symbol string conditions.

9.8.2, Pseudowords and Consonant Strings

As a result of comparisons between the pseudoword condition and the prestimulus baseline, three main effects were observed. Firstly, within the first 200ms of stimulus onset, significant differential effects were observed within the right cerebellum, approximately 400ms later, differential effects were observed within right parietal BA40. Finally, between 500 and 700ms after stimulus onset, significant differential effects were observed within the left middle frontal gyrus (BA46).

There were a number of similarities between these effects, and the main effects that were identified by comparing the consonant string condition with the prestimulus baseline.

As with the pseudoword condition, consonant strings were associated with significant effects within the right cerebellum and right parietal regions.

Both the right cerebellar and right parietal effects were observed approximately 200-300ms later within the consonant string condition than the pseudoword condition. The right parietal effects were observed within the 20-30Hz beta frequency band in the consonant string condition, and within the 40-50Hz gamma band in the pseudoword condition. The right cerebellar effects were observed within alpha/low beta frequency bands (20-30Hz in the case of the consonant string condition, and 8-20Hz for the pseudoword condition).

Unlike the pseudoword condition, the consonant string condition was not associated with significant left frontal effects, but was linked to significant left superior temporal effects within the 40-50Hz gamma frequency band, 500-700ms after stimulus onset. Each of these effects will be considered in turn.

9.8.3. Right cerebellar effects

As discussed within the introduction, although a number of studies have failed to report right cerebellar effects during the processing of nonwords (as shown by the review conducted by Mechelli et. al. 2003), there are reports of right cerebellar effects being linked to pseudoword processing (for example, Mechelli et. al. 2003), and also word processing relative to symbol string processing (Xiang et. al. 2001). As described in Chapter 4, the interpretation of right cerebellar effects, specifically those observed within task manipulation studies, have been wide ranging. For example, right cerebellar effects have been linked to the process of subvocal rehearsal within a sustained search (Desmond et. al. 1998), and also associated with semantic tasks when compared to phonological tasks (Roskies et. al. 2001). The involvement of the right cerebellum within the consonant string and pseudoword condition is consistent with both interpretations, i.e. as either being linked to phonological processes or semantic processes.

Right cerebellar effects reached significance at a later latency within the consonant string condition, compared to the pseudoword condition. It is possible to speculate that this may be indicative of a delayed attempt at lexical/semantic processing once attempts at producing a phonological representation have failed, or that delayed right cerebellar effects

may reflect at attempt at subvocalisation within the consonant string condition, once semantic/lexical processing attempts have failed.

There was also an ERD/ERS dissociation between the right cerebellar effects observed within each of the two stimulus conditions. The right cerebellum was associated with a power decrease relative to the prestimulus baseline (indicative of ERD) within the consonant string condition, and a power increase (indicative of ERS) within the pseudoword condition. There are a number of possible explanations available that could account for the ERS/ERD dissociation between the two stimulus conditions. The possibilities regarding the functional significance of these effects are discussed within Chapter 2 and Chapter 7, and include ERS within phonological condition representing inhibitory effects, or the involvement of more widespread underlying neuronal networks. However, within the study reported by Xiang et. al. (2001), which also employed the use of SAM analysis, the cerebellar effects associated with word viewing took the form of an increase in spectral power (ERS) in four participants, and a decrease in spectral power (ERD) in two participants, suggesting a certain degree of individual variability, which possibly reflects differences in strategy.

9.8.4. Right parietal effects

The significant right parietal ERD effect observed within the pseudoword condition was slightly more superior to that observed within the consonant string condition, although the voxels identified within the two conditions were within approximately 24mm of each other. A significant differential effect was also observed within the left inferior parietal region (BA40), with the pseudoword condition associated with ERD and the consonant string condition associated with ERS. This differential effect occurred early within the epoch (0-200ms) and within the 8-20Hz frequency band.

BA40 within bilateral inferior parietal regions has often been associated with phonological processing tasks, (for example, Mummery et. al. 1998; Otten & Rugg 2001; McDermott et. al. 2003) as discussed within Chapter 4. None of the word conditions were associated with significant effects in this area, suggesting that this region may be linked to phonological processes occurring within the orthographic nonword conditions. The significant right parietal effects observed within the consonant string condition were identified within a later time window (600-800ms) compared to the pseudoword condition (400-600ms). As the mean reaction time for performing the lexical decision task within the

consonant string condition was 575ms, this suggests that the involvement of this region within the consonant string condition may not be necessary for successful completion of the lexical decision task, and that is more likely to be involved in the pseudoword condition.

Therefore, both the results of the task manipulation studies described in Chapter 4, and the latency difference between the pseudoword and consonant string conditions indicate that the right parietal ERD may reflect a greater reliance on phonological processes within the pseudoword condition. This interpretation is directly opposed to that taken by Specht et. al. (2003) in which the performance of a lexical decision task is believed to mainly involve a phonological discrimination processes when the stimuli are nonpronounceable nonwords, and mainly lexical/semantic discrimination processes when the stimuli are pronounceable pseudowords.

9.8.5. Inferior temporal effects

Left inferior temporal and middle temporal differential effects were observed within the pseudoword v consonant string comparison (0-200ms, 20-30Hz), which were associated with enhanced ERD within the consonant string condition. The results obtained from other stimulus comparisons show enhanced inferior temporal ERD within the symbol string condition with respect to the pseudoword condition, within the pseudoword condition relative to the concrete noun condition. Each of these results suggest enhanced inferior temporal ERD associated with the less "word like" stimulus types. These results are also consistent with those reported by Lutzenberger, Pulvermuller & Birbaumer (1994), following an EEG study, in which mean 30Hz responses to words were significantly larger than those observed in response to the presentation of pseudowords (with pseudowords being associated with a significant reduction in 30Hz power), between 320 and 520ms post stimulus onset. Although sources were not localised specifically to inferior temporal regions on the basis of these results, the frequency and latency of this effect is consistent with the inferior temporal effects observed within the present study.

Such inferior temporal regions have been shown to play a role within semantic task processing (Price, 2000; Mummery et. al. 1998), have been described as being part of a "semantic route to reading" (Price, 2000, page 348), and associated with "semantic stores" (Roskies et. al. 2001, page 839). The enhanced ERD within less "word-like" conditions, during the lexical decision task, may therefore reflect an enhanced or more sustained

attempt at lexical/semantic identification within these stimulus conditions, in line with the approach taken by Specht et. al. (2003).

9.8.6, Superior temporal effects

The superior temporal ERD observed within the consonant string condition, in the 500-700ms time window and 40-50Hz frequency band, is consistent with the hypothesis outlined within the introduction, in which performing a lexical decision on nonpronounceable nonwords is believed to involve a greater reliance on phonological processes (Specht et. al. 2003), which are thought to be subserved by left superior temporal regions. This interpretation is in line with the results of task manipulation studies which associated left superior temporal effects with phonological processing conditions (for example, Paulesu, et. al. 1993; Isahai et. al. 2000).

9.8.7, Left middle frontal regions

Significant left middle frontal (BA46) ERD was observed within the pseudoword condition (500-700ms, 40-50Hz). Similar left middle frontal regions were associated with significant ERS within the abstract noun and homograph stimulus conditions. The voxels in which these three effects reached significance were within 18mm of each other.

As with inferior temporal effects, it is possible that the left middle frontal pseudoword ERD may represent an enhanced and more sustained attempt at lexical matching. The functional significance of the ERS observed within the abstract noun and homograph stimulus conditions is unclear, but it is again possible to speculate about a role played by inhibition effects, or differences in terms of the spatial extent of underlying neuronal effects (as done in Chapter 7). It is difficult to relate these effects to those observed within semantic and phonological task manipulation studies, as these results tend to differentiate between more posterior prefrontal regions (e.g. BA44 and BA45), which tend to be associated with phonological tasks, and more anterior regions (e.g. BA47 and BA10), which are linked to semantic task conditions (for example, Fiez, 1997, as discussed within Chapter 4).

9.9, Summary

The reaction time data is in line with the model of lexical decision outlined in figure 9.3 and consistent with the approach taken by Specht et. al. (2003). The MEG study investigated the neural correlates associated with performance of the lexical decision task within each of these stimulus conditions. Results reveal differential effects depending on the "word like" nature of the stimulus.

Attempts were made to interpret the MEG data obtained from this stimulus manipulation study within the context of the model developed from the behavioural data, and the results obtained both from previous task manipulation studies. In line with this model, the symbol string condition was associated with the shortest mean reaction time, and ERD/ERS effects were confined to occipital regions, suggesting that within this condition the lexical decision involves a brief process of visual analysis.

Pseudowords had the longest mean reaction time, and were associated with right cerebellar and right inferior parietal effects, regions which were also associated with significant effects within the consonant string condition. Although interpretation of these effects is ambiguous, they seem to be more closely allied to effects observed within the phonological task condition of the studies reported within Chapter 4. Interpretation of the left superior temporal effects associated with the consonant string condition, and the left middle frontal effects linked to the pseudoword condition is also ambiguous. The most consistent effects were those observed within bilateral inferior temporal regions, in which less "word-like" stimuli tended to be associated with enhanced ERD within the beta frequency range. These inferior temporal regions have often been associated with semantic processing, and described as representing "semantic stores" (Roskies et. al. 2001, page 839), so that the enhanced beta ERD within the less word-like conditions was interpreted as reflecting a greater reliance on lexical/ semantic processing.

Chapter 10

Concluding account.

Within Chapter 3 certain issues relating to language research are discussed, specifically the differentiation between semantic and phonological processing pathways. The importance of combining a cognitive neuroscience approach to language with that of linguistic and psycholinguistic research is also outlined in Chapter 3. The studies described within this thesis used the neuroimaging technique magnetoencephalography, together with behavioural studies, in order to investigate these issues.

By using SAM to analyse the MEG data, spectral power changes were identified which could either have been evoked (phase-locked to the stimulus) or induced by the presence of a stimulus (without phase-locking). This approach is particularly advantageous for the study of language processes for which timing has been found to be inherently variable (Michalewski et. al. 1986). Also, by using SAM analysis to interpret the MEG data it was possible to investigate the neural correlates of semantic and phonological processes within the domains of space, time and frequency.

In order to investigate the neural correlates of semantic and phonological processes, these need to be isolated using experimental manipulations. As discussed within Chapter 3, there have tended to be two approaches taken, i.e. task manipulations and stimulus manipulations. Both approaches have been adopted within this thesis.

As a result of previous research, the left inferior parietal region (BA40) has tended to be linked to the notion of "phonological stores", whereas left temporal regions have been associated with "semantic stores", with left inferior frontal and left superior/middle frontal (BA10) regions being associated with executive control of processes such as selection and retrieval. The cerebellum has been associated with the process of sub-vocal rehearsal.

The study reported within Chapter 5 used task manipulations in order to investigate the neural correlates of semantic and phonological task processing. Results revealed that both task conditions were associated with ERD within the beta and gamma frequency rages, with significant gamma effects confined to the left frontal gyrus (B10) in both cases. This effect occurred earlier within the semantic condition than within the phonological task condition. Within the semantic task condition, in the beta frequency band, statistically

significant ERD was observed within the left middle temporal gyrus (BA39) and the right superior temporal gyrus within the 350-550ms time window, and within the left inferior parietal lobule (BA40) within the later time window of 500-700ms. This parietal effect may be the result of delayed implicit phonological processing as left inferior parietal (BA40) ERD was observed within the earlier 350-550ms time window for the phonological task condition.

Within the beta frequency band, the phonological task condition was associated with left temporal-occipital and left inferior parietal (BA40) effects within the early 350-550ms time window, and left inferior frontal ERD within the later (500-700ms) time window. Right frontal ERD also reached significance at the group level within the 350-550ms window; however, from individual SAM images it seems likely that both frontal and superior temporal ERD contributed to this effect. Cerebellar effects were significant in both time windows within the phonological task condition, supporting the notion that the cerebellum may play a role associated with sub-vocal rehearsal.

In terms of the spatial-temporal dynamics associated with the two task conditions, the main difference was in the relative timings of frontal and temporal/parietal effects. Findings from this study suggest that for the semantic task, the involvement of such frontal executive systems tends to precede that of the temporal "semantic stores". However, within the phonological task condition, left inferior parietal (BA40) ERD preceded the left frontal ERD. These findings therefore indicate that there may be a dissociation between the use of such "stores" within semantic and phonological processing.

In Chapter 7 the neural correlates of semantic and phonological task priming were investigated. Significant task-dependent differential effects were observed in response to the presentation of task instructions, i.e. preceding specific semantic/phonological processing requirements. Furthermore, a number of parallels were identified between the task specific effects associated with the presentation of the task prime and presentation of the target word (when the two task conditions were compared to the prestimulus baseline). This extends the work on the priming of semantic and phonological tasks. It also extends the findings relating to task dependent differential effects observed in response to a task cue, as it considers these effects alongside those associated with task-specific stimulus processing, and identifies a number of parallels between the two.

At certain voxels within the left middle temporal gyrus and left inferior frontal gyrus the onset of the semantic task prime was associated with statistically significant ERD, whereas onset of the phonological task prime task was associated with ERS. Such a dissociation was also observed between the two epoch types. Whereas voxels within the right superior temporal gyrus and the left middle temporal gyrus were associated with significant ERS within the phonological task prime condition, they were associated with significant ERD within the semantic target epoch. Various interpretations for this ERD/ERS dissociation have been discussed.

In terms of language processing, it may be that the process of task-priming, as facilitated by paradigms such as this, could enable the investigation of different processing frameworks (in this case semantic or phonological processing) without the potential drawbacks associated with relying upon data obtained during the processing of different target stimuli, such as the introduction of confounds associated with the choice of target stimuli.

Chapters 5 and 7 report studies in which the neural correlates of semantic and phonological processing were investigated using task manipulations. The study reported in Chapter 9 involved the use of stimulus manipulations in order to study these effects. Within such studies word processing has been compared to the processing of different types of nonwords, for example, symbol strings which have no orthographic, phonological or semantic component, nonpronouncable nonwords which are orthographic but have no recognisable phonological or lexical/semantic component, and pronounceable pseudowords which can be processed phonologically, but have no lexical/semantic component.

There are a number of problems associated with these studies. Firstly, most have examined only evoked responses (which are phase locked to stimulus onset), and are therefore susceptible to distortion and attenuation due to individual variability. The majority also rely on the assumption that certain stimulus types will automatically afford the type of processing to which they are most readily susceptible, regardless of the task conditions. For example, pronouncable pseudowords have been assumed to afford enhanced phonological processing, whereas the presentation of real words has been thought to automatically induce lexical/semantic processing. An alternative approach considers these processing components within the context of a lexical decision process, and asserts that performing a lexical decision on pronounceable pseudowords mainly

involves lexical/semantic discrimination processes, whereas performing this task on nonpronounceable nonwords mainly involves phonological discrimination processes.

Six different stimulus types were presented within the context of a lexical decision task, three were word categories and three were nonword types (pronounceable pseudowords, nonpronouncable consonant strings, and strings of symbols). By using MEG and SAM analysis, it was possible to extend the approach beyond the study of evoked responses, and to investigate ERD and ERS effects that are not necessarily phase-locked to stimulus onset (induced).

By using a lexical decision task an attempt was made to avoid the confounds associated with task requirements such as reading aloud, which may bias phonological processes. However, the use of this task does not exclude the possibility of confounds being introduced. For example, Henson et. al. (2002) stated that word-nonword differences in a lexical decision task could reflect the different decisions (acceptance versus rejection) rather than differences in stimuli per se. It was also believed that the use of a lexical decision task would remove the need to rely on the assumption that the presentation of a certain stimulus type automatically affords a certain type of processing. In a further attempt to overcome the interpretation difficulties discussed previously, a behavioural study was conducted in order to determine mean reaction times for the different stimulus conditions. Results revealed that participants tended to respond to the lexical decision task fastest when presented with symbol strings, and slowest when presented with pseudowords. The MEG data can therefore be interpreted within the context of these reaction time constraints.

MEG results reveal differential effects depending on the "word like" nature of the stimulus within right cerebellar, bilateral parietal, inferior and superior temporal and middle frontal regions. Attempts were made to interpret the MEG data within the context of the reaction time data, the results of previous task manipulation studies, and the results of the task manipulation studies reported in Chapters 5 and 7. The most consistent effect was observed within bilateral inferior temporal regions, where less "word-like" stimuli tended to be associated with enhanced ERD within the beta frequency range. These inferior temporal regions have often been associated with semantic processing, and described as representing "semantic stores", so that the enhanced beta ERD may reflect a greater reliance on lexical/semantic discrimination processes when conducting a lexical decision on less "word-like" stimuli. The functional significance of superior temporal, parietal, right

cerebellar, and left middle frontal effects is ambiguous, which may be due to the many methodological problems associated with the use of stimulus manipulations.

10.1, A comparison between the results obtained within the task manipulation study and the stimulus manipulation study.

Mechelli et. al. (2003) argue that due to the interpretation difficulties (as discussed previously), interpretation of the results of stimulus manipulation studies is reliant on "a prior understanding of which brain areas are involved in semantic, phonological, lexical and sublexical word processing" (page 261). The stimulus manipulation results are therefore considered within the context of the results obtained from the task manipulation studies reported in Chapters 5 and 7. It would also appear to be advantageous to consider the results of stimulus manipulation studies within the context of task manipulation results, as it seems likely that stimulus manipulation studies would be particularly susceptible to confounds associated with the choice of stimuli. For example, words differ from pseudowords not only in terms of their semantic/lexical representation, but also in terms of factors such as familiarity and frequency. Within task manipulation studies the effects of these confounds can be reduced by including the same stimuli within each task condition (as was done within the MEG study reported in Chapter 5).

10.1.1, Cerebellar effects

The significant right cerebellar ERD observed within the consonant string condition was similar to that observed within the phonological task condition (Chapter 5), both in terms of the time window (350-550ms for the phonological task, and 300-500ms for the consonant string condition), and the frequency band (both low beta, 14-20Hz for the phonological task condition, and 20-30Hz for the consonant string condition). The voxel in which significant ERD effects were observed was more medial in the case of the phonological task. The similarity between these two ERD effects may suggest that the right cerebellar involvement in the consonant string condition reflects enhanced or more sustained phonological processing associated with performing the lexical decision task on consonant strings.

10.1.2, Parietal effects

The left parietal differential effects observed within the pseudoword v consonant string comparison were in close proximity to those observed within the phonological task condition, as described in Chapter 5. Significant differential effects were observed within two left inferior parietal voxels, and the voxel in which the most significant differential effects were observed lies within 4mm approximately from a voxel in which significant ERD was observed within the phonological task condition. The significant phonological task effects were observed within a slightly later time window (350-550ms) than the pseudoword/consonant string differential effects (200-400ms), and both effects occurred within the low beta frequency band.

As the differential effect between pseudowords and consonant strings was associated with ERD within the pseudoword condition, and ERS within the consonant string condition, these results suggest a similarity between the left parietal effects observed within the pseudoword condition, and those observed within the phonological task condition. This may support the suggestion that the pseudoword condition involves a greater reliance on phonological processes than the consonant string condition, which is again directly opposed to the approach taken by Specht et. al. (2003), as discussed above. However, until the specific role that is played by these regions is established it seems impossible to draw conclusions regarding the processing involved within each of these stimulus conditions.

10.1.3, Inferior temporal effects

Although there seems to be a relatively high degree of spatial variability associated with the enhanced inferior temporal ERD observed within the consonant string relative to the pseudoword condition, the symbol string relative to the pseudoword condition, and the pseudoword relative to the concrete noun condition, the location of these effects is approximately coincident with that of the left middle temporal differential effects observed within the comparison between the semantic and phonological task priming conditions (as described within Chapter 7). These differential effects were observed within a 200-400ms time window, and a 20-30Hz frequency band, and were associated with enhanced ERD within the semantic task prime condition, which is consistent with the hypothesis that the enhanced ERD within the less "word-like" stimulus conditions reflects a greater reliance on lexical/ semantic processing.

10.1.4, Superior temporal effects

The superior temporal ERD observed within the consonant string condition seems to be most closely aligned (within approximately 17mm) to the task dependent left middle temporal effects observed within the task priming study. These effects were associated with enhanced ERD within the semantic task prime condition. Should these effects be linked, they may suggest a greater involvement of this region within semantic task processes, which is directly opposed to the hypothesis outlined within Chapter 9 whereby these consonant string ERD effects are linked to phonological processes.

10.1.5, Left middle frontal effects

Although the left middle frontal (BA46) voxels identified as showing significant ERD within the pseudoword condition, and those associated with significant ERS within the abstract noun and homograph conditions are bordering more anterior regions, they seem to be more in line with effects observed within the phonological task conditions in the studies reported in Chapters 5 and 7. For example, the voxel in which significant ERS was observed within the abstract noun condition was within approximately 15mm of the voxel in which significant ERD was observed within the phonological task condition (Chapter 5). The ERS observed within the abstract noun condition occurred within an earlier time window (100-300ms) to that in which significant ERD was observed during phonological task processing (500-700ms). The ERS effect was observed within a frequency band of 40-50Hz, and the ERD observed within a 30-40Hz frequency band.

Similarly, the left middle frontal voxel in which significant ERS was observed within the homograph stimulus condition is within 15mm approximately of the voxel in which significant differential effects were observed between the two task prime conditions (Chapter 7). These differential effects were associated with ERS within the phonological task prime condition, but not within the semantic task condition. However, these effects differed in terms of the frequency band in which they were observed (30-40Hz in the case of the task priming effect, and 8-20Hz in the case of the homograph condition). The differential task priming effect also occurred within an earlier time window (0-200ms) compared to the homograph ERS effect (300-500ms).

These findings therefore suggest that the left middle frontal effects may also be involved within phonological task processing, although the specific nature of these effects is unclear, and there are a number of inconsistencies regarding the nature of the observed effect (i.e. ERD/ERS), and the frequency band in which it is observed.

10.2, Summary

In summary, it appears that in some instances it is possible to observe parallels between the ERD/ERS effects observed with the task manipulation studies and those observed within the stimulus manipulation study. Based upon these parallels it is possible to speculate about underlying semantic and phonological processes that may be common to certain task and stimulus conditions. However, it should be noted that there are alternative frameworks within which these results could be interpreted. Although a lexical decision task was used in an attempt to constrain the processing of the different stimulus types within the stimulus manipulation study (e.g. pseudowords, abstract nouns etc.), while certain results are consistent with an interpretation involving different types of discrimination process (e.g. semantic or phonological), other results lend themselves to an interpretation whereby the different types of stimuli automatically afford different degrees of semantic/phonological processing depending upon the extent to which they can be pronounced or semantically interpreted. For example, the former approach would predict that conducting a lexical decision on a pseudoword would require a reliance on semantic discrimination processes, whereas the latter approach would suggest that pseudowords automatically afford a greater reliance on phonological processes.

10.3, Future research

A requirement of future research would be to overcome interpretation difficulties such as those outlined above. For example, by manipulating task demands beyond a lexical decision, it should be possible to estimate the extent to which a certain type of stimulus automatically affords the engagement of semantic and phonological processing pathways, and the extent to which the engagement of these processes is determined by task requirements.

Also, the results of the task priming study indicate that significant task specific effects can be observed in response to the presentation of a task cue, i.e. preceding specific processing requirements. Furthermore, a number of parallels were identified between the

task related differential effects associated with the presentation of the task cue and presentation of the target stimulus. Future work could address the apparently task specific ERD/ERS dissociation observed in response to the presentation of task cues (as described in Chapter 7). By investigating the priming of different tasks, it may be possible to determine the extent to which the ERS associated within the phonological task prime condition is specific to phonological processes, or to inhibition of semantic processes. It would also be interesting to conduct this study using a haemodynamic measure, such as the fMRI BOLD response. For certain tasks ERD has been found to be spatially coincident with an increase in the BOLD response (Singh et. al. 2002). A decrease in the BOLD response coincident with the ERS observed within the phonological task prime condition may suggest a suppression of neural activity within these typically semantic regions, in line with an inhibition interpretation.

Within the studies reported within this thesis, semantic and phonological ERD/ERS effects tended to be observed within beta (14-20Hz and 20-30Hz) and gamma (40-50Hz) frequency bands, which is consistent with the interpretation that high frequency activity is "of particular relevance to cognition" (Pulvermüller, Birbaumer, Lutzenberger & Mohr, 1997) and that "cortical topographies of high-frequency responses contain information about semantic features of words" (Pulvermüller, Preissl, Lutzenberger & Birbaumer, 1996). Although similarities were observed in terms of the frequency bands in which effects were identified (for example, between task prime and target stimulus epochs within Chapter 7), the functional significance of these frequency effects, and the differences between the observed beta/gamma effects, is unclear. With the advent of more powerful computers and signal processing techniques, future work could extend the approach beyond that of identifying the location, frequency bands, and latencies of significant ERD/ERS effects, and investigate the phase relationships between oscillatory activity within different regions (for example, Hadjipapas, Barnes, Holliday & Rippon, 2003).

Appendix 4.1 Results from task manipulation studies showing significant inferior temporal effects associated with a semantic task.

Semantic Inferior temporal						
Reference	Task	Imaging method	Region	BA	TC	Z
Vandenberghe, Price, Wise, Josephs & Frackowiak, 1996	Matching according to meaning and real-life size v matching according to physical stimulus size for words and pictures	PET	Left inferior temporal gyrus	20	-44,-10,-28	
Mummery, Patterson, Hodges & Price, 1998	Colour and location matching for items referred to by visually presented nouns v matching words according to the number of syllables	PET	Left inferior temporal gyrus		-44,-22,-16	3.9
Alexander, Hiltbrunner & Fischer, 1989	Transcortical sensory aphasia - severe comprehension deficit	Lesion	Left inferior-temporal lobe			
Démonet, Chollet, Ramsay, Cardebat, Nespoulous, Wise, Rascol & Frackowiak, 1992	Monitoring auditorily presented concrete nouns according to semantic criteria with the monitoring of pure tones according to their	PET	Left inferior temporal gyri			

	pitch					
Noppeney & Price, 2003	Decisions regard the taste, colour and origin of food items (auditory stimuli) v decision about whether reversed words and meaningless sounds were spoken by a male or female voice	PET	Left inferior temporal		-54,-50,-18	

Appendix 4.2 Results from task manipulation studies showing significant superior/middle temporal effects associated with a semantic task.

Semantic Superior/middle temporal						
Reference	Task	Imaging method	Region	BA	TC	Z
Price, Moore & Frackowiak, 1996	Silent reading v resting with eyes closed	PET	Right middle temporal		54, -48, 4	7.8
Vandenberghe, Price, Wise, Josephs & Frackowiak, 1996	Matching according to meaning and real-life size v matching according to physical stimulus size for words and pictures	PET	Left middle temporal gyrus	21	-42,0,-28	
			Left middle temporal	21	-58,-38,-4	

			gyrus			
Mummery, Patterson, Hodges & Price, 1998	Colour and location matching for items referred to by visually presented nouns v matching words according to the number of syllables	PET	Left middle temporal gyrus		-56,-24,-6	5.1
McDermott, Petersen, Watson & Ojemann, 2003	Attend to the relations between semantically related words v attend to the relations between rhyming words	fMRI	Left superior/middle temporal cortex	22/21	-56,-45,0	
Démonet, Chollet, Ramsay, Cardebat, Nespoulous, Wise, Rascol & Frackowiak, 1992	Monitoring auditorily presented concrete nouns according to semantic criteria with the monitoring of pure tones according to their pitch	PET	Left middle temporal gyrus and superior temporal regions			

Appendix 4.3 Results from task manipulation studies showing significant temporo-parietal effects associated with a semantic task.

Semantic Temporo-parietal						
Reference	Task	Imaging method	Region	BA	TC	Z
Price, Moore & Frackowiak, 1996	Silent reading v resting with eyes closed	PET	Left temporoparietal junction		-58,-42, 16	6
			Right temporoparietal junction		54 -48 20	7.6
Vandenberghe, Price, Wise, Josephs & Frackowiak, 1996	Matching according to meaning and real-life size v matching according to physical stimulus size for words and pictures	PET	Left parietotemporal junction	19/39	-40,-70,24	
			Left hippocampus	34	-18,-16,-12	
Mummery, Patterson, Hodges & Price, 1998	Colour and location matching for items referred to by visually presented nouns v matching words according to the number of syllables	PET	Left temporo-occipito-parietal junction	39	-46,-72,28	6.8
Alexander, Hiltbrunner &	Transcortical sensory aphasia - severe	Lesion	Left inferior-temporal			

Fischer, 1989	comprehension deficit		lobe			
Démonet, Chollet, Ramsay, Cardebat, Nespoulous, Wise, Rascol & Frackowiak, 1992	Monitoring auditorily presented concrete nouns according to semantic criteria with the monitoring of pure tones according to their pitch	PET	Left middle temporal gyrus and superior temporal regions			

Appendix 4.4 Results from task manipulation studies showing significant posterior temporal effects associated with a semantic task.

Semantic Posterior Temporal (fusiform + parahippocampus)						
Reference	Task	Imaging method	Region	BA	TC	Z
Vandenberghe, Price, Wise, Josephs & Frackowiak, 1996	Matching according to meaning and real-life size v matching according to physical stimulus size for words and pictures	PET	Left fusiform gyrus	21/37	-46,-46,-20	
Mummery, Patterson, Hodges & Price, 1998	Colour and location matching for items referred to by visually presented nouns v matching words according to the number of syllables	PET	Left inferior temporal gyrus / fusiform gyrus		-44,-22,-16	3.9

McDermott, Petersen, Watson & Ojemann, 2003	Attend to the relations between semantically related words v attend to the relations between rhyming words	fMRI	Left fusiform gyrus	37	-34,-45,-18	
Noppeney & Price, 2003	Decisions regard the taste, colour and origin of food items (auditory stimuli) v decision about whether reversed words and meaningless sounds were spoken by a male or female voice	PET	Left inferior fusiform		-28,-38,-22	
Wagner, Schacter, Rotte, Koutstaal, Maril, Dale, Rosen & Buckner, 1998	Abstract/concrete decision v uppercase/lowercase decision	fMRI	Parahippocampal gyrus near fusiform gyrus	36/37/ 35	-34,-40,-12	
			Fusiform gyrus	37	-43,-58,-9	
Otten & Rugg, 2001	Living/nonliving decision v attend to a fixation point	fMRI	Fusiform cortex			
Otten & Rugg, 2001	Living/nonliving decision v syllable counting	fMRI	Left parahippocampal cortex			

Appendix 4.5 Results from task manipulation studies showing significant inferior frontal effects associated with a semantic task.

Semantic Inferior frontal						
Reference	Task	Imaging method	Region	BA	TC	Z
Vandenberghe, Price, Wise, Josephs & Frackowiak, 1996	Matching according to meaning and real-life size v matching according to physical stimulus size for words and pictures	PET	Left inferior frontal gyrus	45	-42,22,20	
			Left inferior frontal gyrus	11/47	-16,30,-12	
Mummery, Patterson, Hodges & Price, 1998	Colour and location matching for items referred to by visually presented nouns v matching words according to the number of syllables	PET	Left inferior frontal gyrus	47	-32,18,-16	3.7
			Left medial superior frontal gyrus		-6,58,26	7.2
			Left orbitofrontal gyrus		-14,54,4	4.5
McDermott, Petersen, Watson & Ojemann,	Attend to the relations between semantically related words v attend to the relations between rhyming	fMRI	Left inferior/middle frontal gyrus	47	-43,39,0	

2003	words					
			Left middle/inferior frontal gyrus	47/11	-37,36,-12	
			Left inferior frontal gyrus	44/45	-37,18,18	
				44	-31,3,27	
			Left middle frontal gyrus	6	-34,3,51	
			Right middle/inferior frontal gyrus	46/44/9	52,27,24	
			Medial frontal gyrus (pre-SMA)	6	-7,9,54	
Petersen, Fox, Posner, Mintun & Raichle, 1989	Generate uses v repeat words (visually presented words)	PET	Left dorsolateral prefrontal	45/46/47	20,42,36	
			Left prefrontal cortex		8,38,36	
			Left inferior prefrontal cortex		-6 28 50	
Petersen, Fox, Posner, Mintun & Raichle, 1989	Generate uses v repeat words (auditory word presentation)	PET	Left inferior prefrontal cortex		-6,33,43	

Demb, Desmond, Wagner, Vaidya, Glover & Gabrieli, 1995	Abstract/concrete decision v uppercase/lowercase decision	fMRI	Left inferior frontal sulcus	45/46/ 47/8		
			Left inferior frontal gyrus			
Demb, Desmond, Wagner, Vaidya, Glover & Gabrieli, 1995	Abstract/concrete decision v decision about whether the first and last letters are in alphabetical order	fMRI	Left inferior frontal sulcus			
			Left inferior frontal gyrus			
Noppeney & Price, 2003	Decisions regard the taste, colour and origin of food items (auditory stimuli) v decision about whether reversed words and meaningless sounds were spoken by a male or female voice	PET	Left inferior frontal		-46,24,12	
			Left superior frontal		-8,66,12	
Wagner, Schacter,	Abstract/concrete decision v uppercase/lowercase	fMRI	Posterior and dorsal	44/6	-43,9,34	

Rotte, Koutstaal, Maril, Dale, Rosen & Buckner, 1998	decision		extent of left inferior frontal gyrus			
					-43,13,28	
			Anterior and ventral left inferior frontal gyrus	45/47	-40,22,21	
					-40,31,12	
			Bilateral frontal operculum	47	-28,22,6	
Kapur, Craik, Tulving, Wilson, Houle & Brown, 1994	Living/nonliving decision v decision regarding the presence or absence of the letter "a"	PET	Left inferior frontal gyrus	45/46	38,28,16	
			Left middle frontal gyrus	47/10	28,34,-4	
Otten & Rugg, 2001	Living/nonliving decision v attend to a fixation point	fMRI	Left and medial prefrontal regions			
Otten & Rugg, 2001	Living/nonliving decision v syllable counting	fMRI	Ventral extent of left inferior frontal gyrus			

			and the medial frontal gyrus			
Poldrack, Wagner, Prull, Desmond, Glover & Gabrieli, 1999	Abstract/concrete decision v case judgment	fMRI	Left inferior frontal gyrus	47	-46,20,-3	7.3
					-35,35,-1	4.38
				44	-49,8,26	6.14
				10	-46,50,1	4.41
			Left superior frontal gyrus	10	-23,60,-7	3.82
			Left orbitofrontal cortex	11	-25,50,-16	3.53
			Left superior frontal gyrus	9	-5,50,33	3.22
			Left middle frontal gyrus	6	-39,0,47	2.8
			Right middle frontal gyrus	10	38,50,15	5.91
			Right inferior frontal	45/47	34,20,0	5.06

			gyrus			
				44	52,8,26	4.53
				45	43,35,13	4.24
			Right orbitofrontal cortex	11	7,60,-18	4.72
Poldrack, Wagner, Prull, Desmond, Glover & Gabrieli, 1999	Abstract/concrete decision v Syllable counting	fMRI	Superior frontal gyrus	9	-7,50,31	4.69
			Medial frontal gyrus	8	-4,35,48	4.61
			Left inferior frontal gyrus	44	-53,16,25	3.68
			Left superior frontal gyrus	6	4,20,56	3.39
			Left inferior frontal gyrus	47	-37,28,-9	3.31
					-42,40,-8	2.74
Roskies, Fiez, Balota, Raichle & Petersen, 2001	Determine whether pairs of words are synonyms v determine whether pairs of words rhyme	PET	Left inferior frontal cortex	47	-41,41,-8	

Appendix 4.5 Results from task manipulation studies showing significant anterior cingulate effects associated with a semantic task.

Semantic Anterior Cingulate						
Reference	Task	Imaging method	Region	BA	TC	Z
Petersen, Fox, Posner, Mintun & Raichle, 1989	Generate uses v repeat words	PET	Anterior Cingulate		38,-6,24	
			Inferior Anterior Cingulate		28,-2,34	
Poldrack, Wagner, Prull, Desmond, Glover & Gabrieli, 1999	Abstract/concrete decision v case judgment	fMRI	Anterior Cingulate	32	-1,20,42	6.96
				24/32	-2,8,45	5.09

Appendix 4.6 Results from task manipulation studies showing significant cerebellar effects associated with a semantic task.

Semantic Cerebellum						
Reference	Task	Imaging method	Region	BA	TC	Z
Vandenberghe, Price, Wise, Josephs & Frackowiak, 1996	Matching according to meaning and real-life size v matching according to physical stimulus size for words and pictures	PET	Right cerebellum		38,-76,-48	
McDermott, Petersen, Watson & Ojemann, 2003	Attend to the relations between semantically related words v attend to the relations between rhyming words	fMRI	Right cerebellum		19,-81,-33	
			Left cerebellum		-10,-78,-33	
Petersen, Fox, Posner, Mintun & Raichle, 1989	Generate uses v repeat words	PET	Left cerebellum		-22,16,-64	
					-16,0,-36	
			Right cerebellum		-18,-10,-58	
					-22,-38,-48	
Noppeney & Price, 2003	Decisions regard the taste, colour and origin of food items (auditory stimuli) v decision	PET	Right cerebellum		12,-90,-30	

	about whether reversed words and meaningless sounds were spoken by a male or female voice					
Roskies, Fiez, Balota, Raichle & Petersen, 2001	Determine whether pairs of words are synonyms v determine whether pairs of words rhyme	PET	Right cerebellum		15,-85,-26	

Appendix 4.7 Results from a task manipulation study showing significant anterior cingulate effects associated with a phonological.

Phonological Anterior Cingulate						
Reference	Task	Imaging method	Region	BA	TC	Z
Poldrack, Wagner, Prull, Desmond, Glover & Gabrieli, 1999	Syllable counting v case judgment	fMRI	Anterior Cingulate	24/32	-3,8,36	3.22

Appendix 4.9 Results from task manipulation studies showing significant parietal effects associated with a phonological task.

Phonological Parietal						
Reference	Task	Imaging method	Region	BA	TC	Z
Mummery, Patterson, Hodges & Price, 1998	Matching words according to the number of syllables v colour and location matching for items referred to by visually presented nouns	PET	Left supramarginal gyrus	40	-56,-34,34	6.3
			Right supramarginal gyrus	40	52,-40,46	6.0
McDermott, Petersen, Watson & Ojemann, 2003	Attend to the relations between rhyming words v attend to the relations between semantically related words	fMRI	Right inferior parietal lobule	40	43,-39,45	
			Left superior/inferior parietal lobule	7/40	-31,-57,48	
			Right superior/inferior	7/40	31,-48,51	

			parietal lobule			
Petersen, Fox, Posner, Mintun & Raichle, 1989	Repeating words v attending to a fixation point.	PET	Left temporoparietal cortex		14,54,-30	
Otten & Rugg, 2001	Syllable counting v living/nonliving decision	fMRI	Left parahippocampal cortex			
Paulesu, Frith & Frackowiak, 1993	Memory for visually presented letters v memory for Korean letters	PET	Left supramarginal gyrus	40	-44,-32, 24	
			Right supramarginal gyrus	40	54,-32,24	
Temple, Poldrack, Salidis, Deutsch, Tallal, Merzenich & Gabrieli, 2001	Rhyming letters v matching letters	fMRI	Left central sulcus	1/2/3 /4	-51,-11,31	2.66
			Left postcentral	1/2/3	-52,-21,44	2.47
			Right central sulcus	1/2/3 /4	61,-13,34	2.51

Appendix 4.10 Results from task manipulation studies showing significant frontal effects associated with a phonological task.

Phonological Frontal						
Reference	Task	Imaging method	Region	BA	TC	Z
McDermott, Petersen, Watson & Ojemann, 2003	Attend to the relations between semantically related words v attend to the relations between rhyming words	fMRI	Left inferior frontal/precentral gyri	6/44	-55,3,15	
Otten & Rugg, 2001	Syllable counting v living/nonliving decision	fMRI	Dorsal extent of the left inferior frontal gyrus			
Poldrack, Wagner, Prull, Desmond, Glover & Gabrieli, 1999	Syllable counting v case judgment	fMRI	Left inferior frontal gyrus	45	-47,28,16	2.86
			Left premotor	6	-46,0,24	2.35
			Right middle frontal gyrus	8/9	38,20,33	3.14
			Right inferior	44	60,8,27	2.69

			frontal gyrus			
Poldrack, Wagner, Prull, Desmond, Glover & Gabrieli, 1999	Syllable counting v abstract/concrete decision	fMRI	Left middle frontal gyrus	9/46	-42,35,26	4.02
			Left premotor	6	-47,0,13	3.11
			Right inferior/middle frontal gyrus	45/9	33,20,41	3.17
			Right inferior frontal gyrus	45	48,35,7	3.03
				44	47,8,37	3.00
				10	41,50,2	2.72
			Right superior frontal gyrus	10	27,60,5	2.50
			Right premotor	6	49,0,16	3.68
			Medial frontal gyrus	10	10,50,4	2.94
Paulesu, Frith & Frackowiak, 1993	Rhyming letters v observing Korean letters	PET	Left	44	-46,2,16	

			Right	44	48,4,12	
Temple, Poldrack, Salidis, Deutsch, Tallal, Merzenich & Gabrieli, 2001	Rhyming letters v matching letters	fMRI	Left superior/medial frontal	6	-12,-11,71	3.34
			Left inferior frontal/precentral	6/44	-59,-6,13	2.83

Appendix 4.11 Results from task manipulation studies showing significant temporal effects associated with a phonological task.

Phonological Temporal						
Reference	Task	Imaging method	Region	BA	TC	Z
Paulesu, Frith & Frackowiak, 1993	Rhyming letters v observing Korean letters	PET	Left superior temporal gyrus	22/42	-46,-32,16	
			Right superior temporal gyrus	22/42	50, -28,16	
Temple, Poldrack, Salidis, Deutsch, Tallal, Merzenich & Gabrieli, 2001	Rhyming letters v matching letters	fMRI	Right superior temporal	22/42	67,-10,9	2.14
				22/42	67,-10,9	2.14
			Left middle temporal/angular gyrus	39	-55,-65, 16	2.2.7

Table 4.12 Results from task manipulation studies showing significant insula effects associated with a phonological task.

Phonological Insula						
Reference	Task	Imaging method	Region	BA	TC	Z
Paulesu, Frith & Frackowiak, 1993	Rhyming letters / remembering letters v observing Korean letters	PET	Left insula		-34,2,4	
			Right insula		40,4,4	

Appendix 4.13 Results from task manipulation studies showing significant cerebellar effects associated with a phonological task.

Phonological Cerebellum						
Reference	Task	Imaging method	Region	BA	TC	Z
Paulesu, Frith & Frackowiak, 1993	Rhyming letters / remembering letters v observing Korean letters	PET	Left cerebellum		-18,-54,-16	
			Right cerebellum		14,-60,-16	

Appendix 4.14 Results from task manipulation studies showing significant thalamic effects associated with a phonological task.

Phonological Thalamus						
Reference	Task	Imaging method	Region	BA	TC	Z
Temple, Poldrack, Salidis, Deutsch, Tallal, Merzenich & Gabrieli, 2001	Rhyming letters v matching letters	fMRI	Left thalamus		-20,-13,18	3.17

Appendix 5.1

Living, one syllable	Nonliving, one syllable
crab,	quilt,
ape,	mop,
fox,	rug
bird	tube
finch	clamp
lark	clog
duck	cork
bat	fan
shrew	braid
mole	vest
fly	net
wren	bike
frog	bead
wolf	nail
hawk	purse
whale	fudge
moth	harp
rat	jam
bee	log
stoat	drape
flea	reel
slug	doll
cow	jet
vole	swab
elk	hob
goose	scarf
dog	fig
horse	plane
cub	eel
worm	sock

Living, one syllable	Nonliving, one syllable
baboon	petrol
donkey	puddle
crayfish	padlock
rabbit	pulley
badger	seesaw
cuckoo	sandal
zebra	kiosk
tiger	canoe
chicken	feather
dormouse	flapjack
earwig	saucer
camel	anvil
tortoise	doorstep
giraffe	scooper
cobra	jelly
cheetah	sausage
hedgehog	dumpling
lizard	settee
walrus	wicket
monkey	trifle
maggot	tarmac
panda	visor
heron	ladle
kitten	easel
vulture	bandage
reindeer	fanlight
puffin	trowel
otter	satin
greyhound	footstool
squirrel	scissors
goldfish	bracelet
peacock	biscuit

Appendix 5.2

Living, one syllable	Nonliving, one syllable
plaice	bleach
swan	sash
bull	wax
hen	gin
gnat	kilt
shrimp	trench
pig	pop
jay	bow
lamb	cart
mule	wick
sheep	chart
bear	wage
shark	stile
hare	dart
goat	robe
seal	lamp
rook	pier
snail	flake
cod	jug
deer	arch
carp	hoop
wasp	wand
mouse	spade
swift	drill
fish	tape
ass	mat
crow	kite
toad	vase
ewe	mug
dove	loaf
snake	brush

Living, one syllable	Nonliving, one syllable
beetle	pewter
ferret	cookie
gibbon	pantry
python	shower
blackbird	forecourt
emu	oxo
weasel	parcel
turkey	hammer
lion	fuel
duckling	tweezers
firefly	skittle
dingo	tunic
rooster	printer
hamster	sherbet
beaver	packet
dolphin	chutney
poodle	cinder
leopard	trapeze
llama	laser
parrot	pliers
pony	cave
ostrich	pudding
partridge	hailstone
magpie	staple
eagle	canon
falcon	velvet
piglet	muffin
penguin	toaster
turtle	trophy
porpoise	trombone
skylark	bagpipe
gazelle	sacking
spider	armour

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